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As filed with the Securities and Exchange Commission on February 21, 2018.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

AERPIO PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**61-1547850**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

9987 Carver Road
Cincinnati, OH 45242
(513) 985-1920
(Address, including zip code, and telephone number, including area code, of principal executive offices)

Stephen Hoffman
Chief Executive Officer
9987 Carver Road
Cincinnati, OH 45242
(513) 985-1920
(Name, address, including zip code, and telephone number, including area code, of agent for service)

With copies to:
Kingsley L. Taft, Esq.
Danielle Lauzon, Esq.
Goodwin Procter LLP
100 Northern Avenue
Boston, Massachusetts 02210
(617) 570-1000

Approximate date of commencement of proposed sale to the public: From time to time after this registration statement becomes effective.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: ☒

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☒
		Emerging growth company box	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Unit(2)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee(4)
Common Stock(5)				
Preferred Stock(6)				
Debt Securities(7)				
Warrants(8)				
Units(9)				
Total	$150,000,000	N.A.	$150,000,000	$18,675

(1) The amount to be registered consists of up to $150,000,000 of an indeterminate amount of common stock, preferred stock, debt securities, warrants and/or units. There is also being registered hereunder such currently indeterminate number of (i) shares of common stock or other securities of the registrant as may be issued upon conversion of, or in exchange for, convertible or exchangeable debt securities and/or preferred stock registered hereby, or (ii) shares of preferred stock, common stock, debt securities or units as may be issued upon exercise of warrants registered hereby, as the case may be. Any securities registered hereunder may be sold separately or as units with the other securities registered hereunder.

(2) The proposed maximum aggregate offering price per unit will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the Securities Act.

(3) Estimated solely for purposes of computing the registration fee. No separate consideration will be received for (i) common stock or other securities of the registrant that may be issued upon conversion of, or in exchange for, convertible or exchangeable debt securities and/or preferred stock registered hereby, or (ii) preferred stock, common stock, debt securities or units that may be issued upon exercise of warrants registered hereby, as the case may be.

(4) The registration fee has been calculated in accordance with Rule 457(o) under the Securities Act.

(5) Including such indeterminate amount of common stock as may be issued from time to time at indeterminate prices or upon conversion of debt securities and/or preferred stock registered hereby, or upon exercise of warrants registered hereby, as the case may be.

(6) Including such indeterminate amount of preferred stock as may be issued from time to time at indeterminate prices or upon conversion of debt securities and/or preferred stock registered hereby, or upon exercise of warrants registered hereby, as the case may be.

(7) Including such indeterminate principal amount of debt securities as may be issued from time to time at indeterminate prices or upon exercise of warrants registered hereby, as the case may be.

(8) Including such indeterminate number of warrants or other rights, including without limitation share purchase or subscription rights, as may be issued from time to time at indeterminate prices.

(9) Each unit will be issued under a unit agreement and will represent an interest in two or more securities, which may or may not be separable from one another.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933, AS AMENDED, OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

EXPLANATORY NOTE

This Registration Statement contains the following documents:

- A base prospectus which covers the offering, issuance and sale by us of up to $150,000,000 in the aggregate of the securities identified above from time to time in one or more offerings; and
- A sales agreement prospectus supplement covering the offering, issuance and sale by us of up to a maximum aggregate offering price of $75,000,000 of our common stock that may be issued and sold under a sales agreement with Cantor Fitzgerald & Co, or Cantor Fitzgerald.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The sales agreement prospectus supplement immediately follows the base prospectus. The $75,000,000 of common stock that may be offered, issued and sold under the sales agreement prospectus supplement is included in the $150,000,000 of securities that may be offered, issued and sold by us under the base prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate purchase price of $75,000,000 from time to time through Cantor Fitzgerald. The sales agreement prospectus supplement covers such aggregate amount. Upon termination of the sales agreement with Cantor Fitzgerald & Co., any portion of the $75,000,000 included in the sales agreement prospectus that is not sold pursuant to the sales agreement will be available for sale in other offerings pursuant to the base prospectus, and if no shares are sold under the sales agreement, the full $150,000,000 of securities may be sold in other offerings pursuant to the base prospectus and a corresponding prospectus supplement.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

PRELIMINARY PROSPECTUS (Subject to Completion)
Dated February 21, 2018

$150,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

We may from time to time issue, in one or more series or classes, up to $150,000,000 in aggregate principal amount of our common stock, preferred stock, debt securities, warrants and/or units. We may offer these securities separately or together in units. We will specify in the accompanying prospectus supplement the terms of the securities being offered. We may sell these securities to or through underwriters and also to other purchasers or through agents. We will set forth the names of any underwriters or agents, and any fees, conversions or discount arrangements, in the accompanying prospectus supplement. We may not sell any securities under this prospectus without delivery of the applicable prospectus supplement.

You should read this document and any prospectus supplement or amendment carefully before you invest in our securities.

Our common stock is listed on the OTC Markets—OTCQB Tier, under the symbol “ARPO.” On February 16, 2018, the closing price for our common stock, as quoted on the OTCQB, was $4.50 per share. Our principal executive offices are located at 9987 Carver Road, Cincinnati, OH 45242.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading “*Risk Factors*” contained in this prospectus beginning on page 2 and any applicable prospectus supplement, and under similar headings in the other documents that are incorporated by reference into this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this Prospectus is , 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for an aggregate offering price of up to $150,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” beginning on page 163 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to the “company,” “we,” “us” and “our” refer to Aerpio Pharmaceuticals, Inc.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described below and in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. The risks described below and incorporated herein by reference are not the only ones we face. Additional risks and uncertainties that are not presently known to us or that we currently believe are immaterial may also impair our business operations or financial condition. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks referenced below and described in the documents incorporated herein by reference, including (i) our quarterly reports on Form 10-Q for the quarter ended September 30, 2017, June 30, 2017 and March 31, 2017, each of which is incorporated by reference into this prospectus and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since inception and anticipate that we will continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred net losses each year since our inception, including net losses of $17.0 million and $17.1 million for the years ended December 31, 2016 and 2015, respectively, and $15.2 million for the nine months ended September 30, 2017. As of September 30, 2017, we had an accumulated deficit of $102.3 million. To date, we have not commercialized any products or generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. We do not know whether or when we will generate revenue or become profitable.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through private placements of our preferred stock. The amount of our future net losses will depend, in part, on the rate of our future expenditures, and our financial position will depend, in part, on our ability to obtain funding through equity or debt financings, strategic collaborations or grants. Our lead product candidate, AKB-9778, completed a proof of concept Phase 2 clinical trial in April 2015. Our product candidate AKB-4924 in our HIF-1-a stabilization program recently completed a Phase 1a trial. Our other product candidates are in preclinical development. As a result, we expect that it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market AKB-9778, our future revenues will depend upon the size of any markets in which AKB-9778 has received approval, our ability to achieve sufficient market acceptance, reimbursement from third-party payors and other factors.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase significantly if and as we:

- continue our Phase 2 program and prepare for a future Phase 3 development program of AKB-9778 for the treatment of diabetic retinopathy, or DR, including as we continue our ongoing TIME-2b clinical trial.
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- have our product candidates manufactured for clinical trials and for commercial sale;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;

- initiate additional preclinical, clinical or other studies for AKB-9778, AKB-4924, ARP-1536 and other product candidates that we may develop or acquire;
- seek to discover and develop additional product candidates;
- acquire or in-license other commercial products, product candidates and technologies;
- make royalty, milestone or other payments under any future in-license agreements;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel; and
- create additional infrastructure to support our operations as a public company.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, if at all, we will be able to achieve profitability. If we are required by the United States Food and Drug Administration, or FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

To become and remain profitable, we must succeed in developing and commercializing our product candidates, which must generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable could depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

We will require substantial additional financing. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts.

As of September 30, 2017, our cash and cash equivalents and short-term investments were $24.8 million. We believe that we will continue to expend substantial resources for the foreseeable future developing AKB-9778 and any other product candidates that we may develop or acquire. Additionally, we may expend substantial resources to further develop AKB-4924 if we secure sufficient additional funding, likely from a strategic and commercial partner for that candidate, as well as ARP-1536 if we secure sufficient additional funding, which may be from a partner for that candidate. These expenditures will include costs associated with research and development, potentially obtaining regulatory approvals and having our products manufactured, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our current and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates.

Our future capital requirements depend on many factors, including:

- the rate of progress, results and cost of completing our Phase 2 program of AKB-9778 and our operating costs incurred as we conduct these trials and through our end of Phase 2 meeting with the FDA, and equivalent meetings with the EMA and other regulatory authorities;
- assuming AKB-9778 advances to Phase 3 clinical trials, the scope, size, rate of progress, results and costs of initiating and completing our Phase 3 development program of AKB-9778;
- assuming favorable clinical results, the cost, timing and outcome of our efforts to obtain marketing approval for AKB-9778 in the United States, Europe and in other jurisdictions, including to fund the preparation and filing of regulatory submissions for AKB-9778 with the FDA, the EMA and other regulatory authorities;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials that we may undertake for AKB-4924, ARP-1536 and any other product candidates that we may develop or acquire;
- the timing of, and the costs involved in, obtaining regulatory approvals for AKB-4924 and ARP-1536 if we continue their further development upon securing sufficient additional funding and/or a strategic and commercial partner, and clinical trials of these product candidates are successful;
- the cost and timing of future commercialization activities for our products, if any of our product candidates are approved for marketing, including product manufacturing, marketing, sales and distribution costs;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the cost of having our product candidates manufactured for clinical trials in preparation for regulatory approval and in preparation for commercialization;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such agreements; and
- the costs involved in preparing, filing, prosecuting patent applications, maintaining, defending and enforcing our intellectual property rights, including litigation costs and the outcome of such litigation.

Based on our current operating plan, and absent any future financings or strategic partnerships, we believe that our existing cash and cash equivalents and investments will be sufficient to fund our projected operating expenses and capital expenditure requirements into the fourth quarter of fiscal year 2018. However, our operating plan may change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for AKB-9778, AKB-4924, ARP-1536 or any other product candidates that we develop or acquire, or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to product candidates on unfavorable terms to us.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and license, development and commercialization agreements with collaborators. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other

preferences and anti-dilution protections that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take certain actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through strategic collaborations with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams, research programs or product candidates or grant licenses on terms that are not favorable to us. If we are unable to raise additional funds through equity or debt financing when needed, we may be required to delay, limit, reduce or terminate our product development or commercialization efforts for AKB-9778 and, if we secure sufficient additional funding and/or a strategic and commercial partner, to continue their development, for AKB-4924, ARP-1536 or any other product candidates that we develop or acquire, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We commenced active operations in 2011, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials. We currently have three product candidates, one of which is in preclinical development. Of these product candidates, we may further develop AKB-4924 and ARP-1536 only if we secure sufficient additional funding and/or a strategic and commercial partner, to continue their clinical development. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Only a small fraction of biopharmaceutical development programs ultimately result in commercial products or even product candidates and a number of events could delay our development efforts and negatively impact our ability to obtain regulatory approval for, and to manufacture, market and sell, a product. We have not yet demonstrated our ability to successfully complete later stage clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to expand our capabilities to support commercial activities. We may not be successful in adding such capabilities.

Risks Related to Our Business and the Clinical Development, Regulatory Review and Approval of Product Candidates

We depend heavily on the success of one product candidate, AKB-9778, which is in Phase 2 clinical development. Even if we obtain favorable clinical results, we may not be able to obtain regulatory approval for, or successfully commercialize, AKB-9778.

We currently have only one product candidate, AKB-9778, in clinical development, and our business depends almost entirely on the successful clinical development, regulatory approval and commercialization of that product candidate, which may never occur. We currently have no products for sale, generate no revenues from sales of any drugs, and may never be able to develop marketable products. AKB-9778, which completed a proof of concept Phase 2 clinical trial in April 2015, will require substantial additional clinical development, testing, manufacturing process development, and regulatory approval before we are permitted to commence its commercialization. In June 2017, we announced the initiation of patient dosing in our ongoing Phase 2b clinical trial of AKB-9778 in patients with DR. Additionally, in July 2017 we announced the completion of a single-center study of the safety and efficacy of treatment with concomitant anti-VEGF therapy. Our other product candidate, AKB-4924, recently completed a Phase 1a trial. We currently may further develop AKB-4924 only if we secure sufficient additional funding, likely from a strategic and commercial partner, to continue its

development. In addition, we currently may further develop ARP-1536 only if we secure sufficient additional funding, which may be from a strategic and commercial partner to continue its clinical development. There can be no assurance that we will be able to secure such additional funding or a strategic or commercial partner on commercially reasonable terms or at all. Any failure to do so would impair our ability to advance AKB-4924 and ARP-1536, resulting in our even greater dependence on AKB-9778. None of our product candidates has advanced into a pivotal trial, and it may be years before such trial is initiated, if ever. The clinical trials of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical testing and clinical trials that any drug candidate is safe and effective and any biological product candidate is safe, pure, and potent for use in each target indication. This process can take many years. Of the large number of drugs in development in the United States, only a small percentage successfully complete the FDA regulatory approval process and are commercialized. Accordingly, even if we are able to obtain the requisite capital to continue to fund our development and clinical programs, we may be unable to successfully develop or commercialize AKB-9778.

We are not permitted to market AKB-9778 in the United States until we receive approval of an NDA from the FDA, or in any foreign countries until we receive the requisite approval from such countries. As a condition to submitting an NDA to the FDA for AKB-9778 regarding its ability to treat patients with DR, we must complete our ongoing clinical trials, Phase 3 trials, and any additional non-clinical studies or clinical trials required by the FDA. To date, we have only completed a Phase 2 clinical trial for AKB-9778 and five other early stage trials. AKB-9778 may not be successful in clinical trials or receive regulatory approval. Further, AKB-9778 may not receive regulatory approval even if it is successful in clinical trials. Obtaining approval of an NDA is a complex, lengthy, expensive and uncertain process that typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, the policies or regulations, or the type and amount of clinical data necessary to gain approval, may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that AKB-9778 will never obtain regulatory approval. The FDA may delay, limit or deny approval of AKB-9778 for many reasons, including, among others:

- we may not be able to demonstrate that AKB-9778 is safe and effective in treating patients with DR to the satisfaction of the FDA;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA for marketing approval;
- the FDA may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA may not approve the formulation, labeling or specifications of AKB-9778;
- the FDA may require that we conduct additional clinical trials;
- the contract research organizations, or CROs, that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- we may fail to perform in accordance with the FDA's good clinical practice, or GCP, requirements;
- the FDA may disagree with our interpretation of data from our preclinical studies and clinical trials;
- the FDA may find deficiencies with the manufacturing processes or facilities of third-party manufacturers with which we contract; or
- the policies or regulations of the FDA may significantly change in a manner that renders our clinical data insufficient for approval, or requiring that we amend or submit new clinical protocols.

In addition, similar reasons may cause the EMA or other regulatory authorities to delay, limit or deny approval of AKB-9778 outside the United States.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully market AKB-9778. Because our business is almost entirely dependent upon AKB-9778, any such setback in our pursuit of regulatory approval would have a material adverse effect on our business and prospects.

Alternatively, even if we obtain regulatory approval, that approval may be for indications or patient populations that are not as broad as we intend or desire or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional, unanticipated clinical trials to obtain approval or be subject to additional post marketing testing requirements to maintain regulatory approval. In addition, regulatory authorities may withdraw their approval of a product or the FDA may require a risk evaluation and mitigation strategy, or REMS, for a product, which could impose restrictions on its distribution. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

We have not obtained agreement with the FDA, EMA or other regulatory authorities on the design of our Phase 3 development program.

We have not obtained agreement with the FDA on the design of our Phase 3 development program. We plan to hold an end of Phase 2 meeting with the FDA upon successful completion of our Phase 2 clinical program. If the FDA determines that the Phase 2 trial results do not support moving into a pivotal program, we would be required to conduct additional Phase 2 studies. Alternatively, the FDA could disagree with our proposed design of our Phase 3 development program and could suggest a larger number of subjects or a longer course of treatment than our current expectations. If the FDA takes such positions, the costs of our AKB-9778 development program could increase materially and the potential market introduction of AKB-9778 could be delayed or we could risk not obtaining FDA approval even if the Phase 3 trials meet their primary endpoints. The FDA also may require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will consider an NDA application.

While we intend to follow the regulatory pathway that ranibizumab and aflibercept undertook when they were approved for DR in the presence of DME, we have not yet sought guidance for the regulatory path for AKB-9778 with the EMA or other regulatory authorities. We cannot predict what additional requirements may be imposed by these regulatory authorities or how such requirements might delay or increase costs for our planned Phase 3 development program. For example, ranibizumab and aflibercept are anti-vascular endothelial growth factor, or anti-VEGF therapies, which block vascular endothelial growth factor, used in the treatment of DR, DME, age-related macular degeneration and retinal vein occlusion, while AKB-9778 is a small molecule activator of the Tie-2 pathway, and such differences may result in a different regulatory pathway for AKB-9778, including one that may be longer, more complex or expensive than that of ranibizumab or aflibercept. Because our business is almost entirely dependent upon the successful development, regulatory approval, and commercialization of AKB-9778, any such delay or increase costs would have an adverse effect on our business.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates. Our competitors may have ongoing clinical trials for product candidates that could be competitive with our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. For example, while we have initiated patient dosing in our TIME-2b clinical trial, there is no guarantee that we can successfully enroll patients in a timely manner. As a result, the timeline for recruiting patients, conducting trials and obtaining

regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our development of AKB-9778 or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials and clinicians' and patients' perceptions as to the potential advantages of AKB-9778 in relation to available therapies or other products under development;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.

We may not be able to comply with requirements of foreign jurisdictions in conducting trials outside of the United States. In addition, we may not be able to obtain regulatory approval in foreign jurisdictions.

If AKB-9778 is successful in Phase 2 development, we currently expect to conduct our Phase 3 clinical trial of AKB-9778 that may include trial sites outside of the United States, including Japan and the European Union, and seek regulatory approval for AKB-9778 for the treatment of patients with DR in major markets in addition to the United States, including the European Union. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country, should we attempt to do so, is subject to numerous risks unique to conducting business in international markets, including:

- difficulty in establishing or managing relationships with qualified CROs and physicians;
- different local standards for the conduct of clinical trials;
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatments; and
- the acceptability of data obtained from trials conducted in the United States to the EMA and other regulatory authorities.

If we fail to successfully meet requirements for the conduct of clinical trials outside of the United States, we may be delayed in obtaining, or be unable to obtain, regulatory approval for AKB-9778 in countries outside of the United States.

Regulatory authorities outside the United States will require compliance with numerous and varying regulatory requirements. The approval procedures vary among jurisdictions and may involve requirements for additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. In addition, in many countries outside the United States, a product must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products is also subject to approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval in another jurisdiction. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market.

Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from Phase 1 and Phase 2 clinical trials of AKB-9778 are not necessarily predictive of the results of our completed and any future clinical trials of AKB-9778. If we cannot replicate the positive results from our Phase 1 and Phase 2 clinical trials of AKB-9778 in our ongoing and subsequent clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize AKB-9778.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies may not be predictive of similar results in humans during clinical trials, and successful results from early or small clinical trials may not be replicated in later and larger clinical trials. For example, our early encouraging preclinical and clinical results for AKB-9778 do not ensure that the results of our ongoing clinical trials, including TIME-2b, or any future clinical trials will demonstrate similar results. Our planned Phase 2 and Phase 3 development program will enroll a larger number of subjects and will treat subjects for longer periods than our prior trials, which will result in a greater likelihood that adverse events may be observed. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early stage development, and we may face similar setbacks. If the results of our ongoing or future clinical trials for AKB-9778 are inconclusive with respect to efficacy, if we do not meet our clinical endpoints with statistical significance, or if there are safety concerns or adverse events, we may be prevented from or delayed in obtaining marketing approval for AKB-9778.

We may experience delays in our planned Phase 2 clinical trial for AKB-9778 and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all.

Clinical trials can be delayed or aborted for a variety of reasons, including delay or failure to:

- obtain regulatory approval to commence a clinical trial;
- reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtain institutional review board, or IRB, approval at each site;
- recruit, enroll and retain patients through the completion of clinical trials;
- maintain clinical sites in compliance with trial protocols and regulatory requirements through the completion of clinical trials;
- address any patient safety concerns that arise during the course of the trial;
- initiate or add a sufficient number of clinical trial sites; or
- manufacture sufficient quantities of our product candidate for use in clinical trials.

We could encounter delays if a clinical trial is suspended or terminated by us, by the relevant IRBs at the sites at which such trials are being conducted, by the Data Safety Monitoring Board, or DSMB, for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or lack of adequate funding to continue the clinical trial. Any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly.

Even if we receive regulatory approval for our product candidates, such products will be subject to ongoing regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the products. In addition, if the FDA approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practice, or cGMP, requirements and GCP requirements for any clinical trials that we conduct post-approval.

Post-approval discovery of previously unknown problems with an approved product, including adverse events of unanticipated severity or frequency or relating to manufacturing operations or processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or product recalls;
- fines, untitled or warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications submitted by us, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- a REMS program; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or are not able to maintain regulatory compliance, we may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct preclinical studies and clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates.

We rely on third party CROs and other third parties to assist in managing, monitoring and otherwise carrying out our ongoing trials of AKB-9778. We expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our clinical trials in the future, including our Phase 3 development program for AKB-9778. We compete with many other companies for the resources of these third parties. The third parties on whom we rely may terminate their engagements with us at any time, and having to enter into alternative arrangements would delay development and commercialization of our product candidates.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP requirements, for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we are responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our investigators or CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or other regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, our clinical trials must be conducted with product produced under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If these third parties do not successfully carry out their duties under their agreements, if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to clinical trial protocols or to regulatory requirements, or if they otherwise fail to comply with clinical trial protocols or meet expected deadlines, the clinical trials of our product candidates may not meet regulatory requirements. If clinical trials do not meet regulatory requirements or if these third parties need to be replaced, preclinical development activities or clinical trials may be extended, delayed, suspended or terminated. If any of these events occur, we may not be able to obtain regulatory approval of our product candidates on a timely basis or at all.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We intend to rely on third parties to conduct some or all aspects of our product manufacturing, and these third parties may not perform satisfactorily.

We do not have any manufacturing facilities and do not expect to independently conduct our product candidate manufacturing for research and preclinical and clinical testing. We currently rely, and expect to rely, on third parties to manufacture and supply drug products for our AKB-9778 clinical trials, and we expect to continue to rely on third parties for the manufacture of clinical and, if necessary, commercial quantities of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

Any of these third parties may terminate their engagement with us at any time. We believe we have sufficient drug product to complete our ongoing trials of AKB-9778. We have entered into an agreement for the manufacturing of the drug substance for the Phase 2 development program of AKB-9778. However, if this manufacturer cannot perform as agreed, we may be required to find replacement manufacturers. We do not currently have arrangements in place for the manufacturing of drug product for the Phase 3 development program. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such replacement, as well as producing the drug product. The FDA or comparable foreign regulatory authorities may find deficiencies with the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies. Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. In addition, we have to enter into technical transfer agreements and share our know-how with the third-party manufacturers, which can be time-consuming and may result in delays. These delays could result in a suspension of our clinical trials or, if AKB-9778 is approved and marketed, a failure to satisfy patient demand.

Reliance on third party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third party manufacturers for all aspects of manufacturing activities, including regulatory compliance and quality assurance;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- disruptions to the operations of our manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or affect our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

The facilities used by our contract manufacturers to manufacture our product candidates must be evaluated by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers for compliance with cGMP requirements for manufacture of both drug substance and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, we will not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, EMA or other regulatory authorities find deficiencies with or do not approve these facilities for the manufacture of our product candidates or if they find deficiencies or withdraw any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Moreover, our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license

revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drug products or product candidates.

In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. Certain of these manufacturing facilities may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

If we are unable to manufacture our product candidates in sufficient quantities, at sufficient yields, we may experience delays in product development, clinical trials, regulatory approval and commercial distribution.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture our product candidates at sufficient yields and at commercial scale. We have limited experience manufacturing, or managing third parties in manufacturing, any of our product candidates in the volumes that will be necessary to support large-scale clinical trials or commercial sales. Efforts to establish these capabilities may not meet initial expectations as to scheduling, scale-up, reproducibility, yield, purity, cost, potency or quality.

Our reliance on contract manufacturers may adversely affect our operations or result in unforeseen delays or other problems beyond our control. Because of contractual restraints and the limited number of third-party manufacturers with the expertise and facilities to manufacture our bulk drug product on a commercial scale, replacement of a manufacturer may be expensive and time-consuming and may cause interruptions in the production of our drug product. A third-party manufacturer may also encounter difficulties in production. These problems may include:

- difficulties with production costs, scale-up and yields;
- availability of raw materials and supplies;
- quality control and assurance;
- shortages of qualified personnel;
- compliance with strictly enforced federal, state and foreign regulations that vary in each country where a product might be sold; and
- lack of capital funding.

Any delay or interruption in our supply of product candidates could have a material adverse effect on our business, financial condition, results of operations and cash flows.

We may not be successful in establishing and maintaining strategic collaborations, which could adversely affect our ability to develop and commercialize our product candidates, negatively impacting our operating results.

If approved, we plan to commercialize AKB-9778 ourselves in the United States and intend to seek one or more strategic collaborators to commercialize AKB-9778 in additional markets. In addition, we may further develop and, if approved, commercialize, AKB-4924 only if we secure sufficient additional funding, likely from a strategic and commercial partner for that candidate. With respect to ARP-1536, we may further develop and, if approved, commercialize ARP-1536 only if we secure sufficient additional funding, which may be from a

strategic or commercial partner. There can be no assurance that we will be able to secure such additional funding or a strategic or commercial partner on commercially reasonable terms or at all. We face competition in seeking appropriate collaborators for our product candidates, and the negotiation process is time-consuming and complex. In order for us to successfully collaborate with a third party on our product candidates, potential collaborators must view these product candidates as economically valuable. Even if we are successful in our efforts to establish strategic collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such strategic collaborations if, for example, development or approval of a product is delayed or sales of an approved product are disappointing. Any delay in entering into strategic collaboration agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market.

In addition, our strategic collaborators may terminate any agreements they enter into with us, and we may not be able to adequately protect our rights under these agreements. Furthermore, our strategic collaborators will likely negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do.

If we fail to establish and maintain strategic collaborations related to our product candidates for the indications and in the geographies in which we do not intend develop and commercialize ourselves, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise. This could negatively affect the development of any product candidate for which we do not locate a suitable strategic partner.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. We will only be able to protect our product candidates, proprietary technologies and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

Composition-of-matter patents on the active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. Method-of-use patents protect the use of a product for the specified method.

This type of patent does not prevent a competitor from making and marketing a product that is identical to our products for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products “off-label.” Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or license may fail to result in issued patents in the United States or in other foreign countries. Even if the patents do successfully issue, third parties may challenge the validity, enforceability, inventorship, or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patent applications we hold with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, and threaten

our ability to commercialize, our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, for applications in which all claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third-party or instituted by the United States Patent and Trademark Office or the USPTO, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. For applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law with the passage of the America Invents Act (2011), which brings into effect significant changes to the U.S. patent laws and which introduces new procedures for challenging pending patent applications and issued patents. A primary change under this reform is creating a “first to file” system in the United States. This will require us to be cognizant of the time from invention to filing of a patent application.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

We currently have a non-exclusive license to one U.S. patent. We rely on the licensor to maintain this patent and otherwise protect the intellectual property covered by this non-exclusive license. We have limited control over these activities or over any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that activities by the licensor have been or will be conducted in compliance with applicable laws and regulations. We may have no control or input over whether, and in what manner, our licensor may enforce or defend the patent against a third-party. The licensor may enforce or defend the patent less vigorously than if we had enforced or defended the patent ourselves. Further, the licensor may not necessarily seek enforcement in scenarios in which we would feel that enforcement was in our best interests. For example, the licensor may not enforce the patent against a competitor of ours who is not a direct competitor of the licensor. If our in-licensed intellectual property is found to be invalid or unenforceable, then the licensor may not be able to enforce the patent against a competitor of ours. Our non-exclusive license does not prevent a third party from seeking and obtaining a non-exclusive license to the same patent that we license. If we fail to meet our obligations under the non-exclusive license agreement, then the licensor may terminate the license agreement. If the license agreement is terminated, the former licensor may seek to enforce the intellectual property against us. We may choose to terminate the license agreement, and doing so would allow a third party to seek and obtain an exclusive license to the patent. If a third party obtains an exclusive license to intellectual property formerly licensed to us, then the third party may seek to enforce the intellectual property against us.

Our patents covering one or more of our products or product candidates could be found invalid or unenforceable if challenged.

Any of our intellectual property rights could be challenged or invalidated despite measures we take to obtain patent and other intellectual property protection with respect to our product candidates and proprietary

technology. For example, if we were to initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable. In patent litigation in the U.S. and in some other jurisdictions, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld material information from the USPTO or the applicable foreign counterpart, or made a misleading statement, during prosecution. A litigant or the USPTO itself could challenge our patents on this basis even if we believe that we have conducted our patent prosecution in accordance with the duty of candor and in good faith. The outcome following such a challenge is unpredictable.

With respect to challenges to the validity of our patents, for example, there might be invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on a product candidate. Even if a defendant does not prevail on a legal assertion of invalidity and/or unenforceability, our patent claims may be construed in a manner that would limit our ability to enforce such claims against the defendant and others. The cost of defending such a challenge, particularly in a foreign jurisdiction, and any resulting loss of patent protection could have a material adverse impact on one or more of our product candidates and our business. Enforcing our intellectual property rights against third parties may also cause such third parties to file other counterclaims against us, which could be costly to defend, particularly in a foreign jurisdiction, and could require us to pay substantial damages, cease the sale of certain products or enter into a license agreement and pay royalties (which may not be possible on commercially reasonable terms or at all). Any efforts to enforce our intellectual property rights are also likely to be costly and may divert the efforts of our scientific and management personnel.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor’s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor’s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Third-party claims of intellectual property infringement may be costly and time consuming, and may delay or harm our drug discovery and development efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. The pharmaceutical and biotechnology industries are characterized by extensive litigation over patent and other intellectual property rights. We may become a party to, or threatened with, future adversarial litigation or other proceedings regarding intellectual property rights with respect to our drug candidates. As the pharmaceutical and biotechnology industries expand and more patents are issued, the risk increases that our drug candidates may give rise to claims of infringement of the patent rights of others.

While our product candidates are in preclinical studies and clinical trials, we believe that the use of our product candidates in these preclinical studies and clinical trials in the United States falls within the scope of the exemptions provided by 35 U.S.C. Section 271(e), which provides that it shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention solely for uses reasonably related to the development and submission of information to the FDA. As our product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We attempt to ensure that our product candidates and the methods we employ to manufacture them, as well as the methods for their use we intend to promote, do not infringe other parties' patents and other proprietary rights. There can be no assurance they do not, however, and competitors or other parties may assert that we infringe their proprietary rights in any event.

Third parties may hold or obtain patents or other intellectual property rights and allege in the future that the use of our product candidates infringes these patents or intellectual property rights, or that we are employing their proprietary technology without authorization. Under U.S. law, a party may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and nonobvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method.

There may be patents of third parties of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. Also, because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. Notwithstanding the above, third parties may in the future claim that our product candidates and other technologies infringe upon these patents and may file suit against us.

Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize AKB-9778 or AKB-4924. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or our intended methods of use, the holders of any such patent may be able to block or impair our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires or is finally determined to be held invalid or unenforceable. We may also elect to enter into a license in order to settle litigation or in order to resolve disputes prior to litigation. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. Should a license to a third-party patent become necessary, we cannot predict whether we would be able to obtain a license, or if a license were available, whether

it would be available on commercially reasonable terms. If such a license is necessary and a license under the applicable patent is unavailable on commercially reasonable terms, or at all, our ability to commercialize our product candidates may be impaired or delayed, which could in turn significantly harm our business.

Further, defense of infringement claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties or redesign our products, which may be impossible or require substantial time and monetary expenditure.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, trademarks, copyrights or other intellectual property. To counter infringement or other violations, we may be required to file claims, which can be expensive and time consuming. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights. In addition, in a patent infringement proceeding, a court may decide that one or more of the patents we assert is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to prevent the other party from using the technology at issue on the grounds that our patents do not cover the technology. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In such a case, we could ultimately be forced to cease use of such marks. In any intellectual property litigation, even if we are successful, any award of monetary damages or other remedy we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment (such as annuities) and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We have received confidential and proprietary information from collaborators, prospective licensees and other third parties. In addition, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of these third parties or our employees' former employers. We may also be subject to claims that former employees, collaborators or

other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our drug candidates. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against these claims, litigation could result in substantial cost and be a distraction to our management and employees.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other countries. Competitors may use our technologies in countries where we have not obtained patent protection to develop their own products and further, may infringe our patents in territories where we have patent protection, but enforcement is not as strong as in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks Related to Commercialization

Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and others in the medical community.

Even if we obtain marketing approval for AKB-9778, AKB-4924 or any other product candidates that we may develop or acquire in the future, these product candidates may not gain market acceptance among physicians, third-party payors, patients and others in the medical community. In addition, market acceptance of any approved products depends on a number of other factors, including:

- the efficacy and safety of the product, as demonstrated in clinical trials;
- the clinical indications for which the product is approved and the label approved by regulatory authorities for use with the product, including any warnings that may be required on the label;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety and efficacy of treatment in relation to alternative treatments;

- the availability of adequate coverage and reimbursement by third party payors and government authorities;
- relative convenience and ease of administration;
- the prevalence and severity of adverse side effects;
- the effectiveness of our sales and marketing efforts; and
- the restrictions on the use of our products together with other medications, if any.

For example, the current established treatments for DME are anti-VEGF medications, including bevacizumab and ranibizumab, and the current established treatments for DR in the absence of DME include laser photocoagulation. We believe that that prescribers may be resistant to prescribing AKB-9778 with or instead of anti-VEGF medications, or instead of laser photocoagulation, which is currently the standard of care for DME and DR, respectively.

Market acceptance is critical to our ability to generate significant revenue. In addition, any product candidate, if approved and commercialized, may be accepted in only limited capacities or not at all. If any approved products are not accepted by the market at all or to the extent that we expect, we may not be able to generate significant revenue and our business would suffer.

If we are unable to establish sales, marketing and distribution capabilities or to enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements with third parties to perform these services.

There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force are expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage geographically dispersed sales and marketing team;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and have to enter into arrangements with third parties to perform these services, our profitability, if any, is likely to be materially diminished in relation to if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute

our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

Coverage and reimbursement may be limited or unavailable in certain market segments for any approved products, which could make it difficult for us to sell our products profitably.

Market acceptance and sales of any approved products will depend significantly on the availability of adequate coverage and reimbursement from third-party payors and may be affected by existing and future healthcare reform measures. Government authorities and third-party payors decide which drugs they will pay for and establish formularies and reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor. Additionally, we may be required to enter into contracts with third-party payors to obtain favorable formulary status. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Even if we obtain coverage for our product candidates, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products. In addition, in the United States third-party payors are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement of new drugs. As a result, significant uncertainty exists as to whether and how much third-party payors will reimburse patients for their use of newly approved drugs, which in turn will put pressure on the pricing of drugs.

Price controls may be imposed, which may adversely affect our future profitability.

In some countries, particularly member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

The impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, also called the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of products, we expect that there will be additional pressure to reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies may be enacted in international markets which could similarly impact our business.

In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively ACA, was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The ACA, among other things, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs and biologic products, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. The U.S. House of Representatives passed legislation known as the American Health Care Act of 2017 in May 2017. More recently, the Senate Republicans introduced and then updated a bill to replace without companion legislation to replace it, and a “skinny” version of the Better Care Reconciliation Act of 2017. Each of these measures was rejected by the full U.S. Senate. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the

government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any products for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenues and achieve or maintain profitability; and
- the level of taxes that we are required to pay.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

The development and commercialization of new products is highly competitive. Our future success depends on our ability to demonstrate and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to develop and commercialize new products with superior efficacy, convenience, tolerability and safety. In many cases, the products that we commercialize will compete with existing, market-leading products.

If AKB-9778 is approved and launched commercially, competing drugs may include current anti-VEGF drugs, including Lucentis, Eylea and Avastin in the treatment of DME, and current therapies including laser photocoagulation in the treatment of DR. We may face competition from potential DME and DR treatments.

Many of our potential competitors have significantly greater financial, manufacturing, marketing, drug development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients and in manufacturing pharmaceutical products. Large and established companies such as Roche and Regeneron, among others, compete in the market for products to treat DR and DME. In particular, these companies have greater experience and expertise in securing government contracts and grants to support their research and development efforts, conducting testing and clinical trials, obtaining regulatory approvals to market products, manufacturing such products on a broad scale and marketing approved products. These companies also have significantly greater research and marketing capabilities than we do and may also have products that have been approved or are in late stages of development, and have collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product that we develop obsolete. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA approval or discovering, developing and commercializing products before, or more effectively than, we do. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. If we are not able to compete effectively against potential competitors, our business will not grow and our financial condition and operations will suffer.

Our products may cause undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our products or even competing products in development that utilize a common mechanism of action could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities and potential products liability claims. AKB-9778 is currently in Phase 2 clinical development. Serious adverse events deemed to be caused by our product candidates could have a material adverse effect on the development of our product candidates and our business as a whole. The most common drug-related adverse events to date in the clinical trial

evaluating the safety and tolerability of AKB-9778 in DME have been dizziness and asymptomatic decreases in blood pressure. Our understanding of the relationship between AKB-9778 and these events, as well as our understanding of adverse events in future clinical trials of other product candidates, may change as we gather more information, and additional unexpected adverse events may be observed.

If we or others identify undesirable side effects caused by our product candidates either before or after receipt of marketing approval, a number of potentially significant negative consequences could result, including:

- our clinical trials may be put on hold;
- patient recruitment could be slowed, or enrolled patients may not want to complete a clinical trial;
- we may be unable to obtain regulatory approval for our product candidates or regulatory authorities may withdraw approvals of product candidates;
- regulatory authorities may require additional warnings on the label;
- a medication guide outlining the risks of such side effects for distribution to patients may be required;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our products and could substantially increase commercialization costs.

Risks Related to Our Business and Industry

If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our products, conduct our clinical trials and commercialize our product candidates.

We are highly dependent on members of our senior management, including Stephen Hoffman, our Chief Executive Officer, Michael Rogers, our Chief Financial Officer, Joseph Gardner, our President and Founder and former Chief Executive Officer, Kevin G. Peters, our Chief Scientific Officer and Stephen Pakola, our Chief Medical Officer. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Our employees, independent contractors, principal investigators, contract research organizations, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk that our employees, independent contractors, principal investigators, contract research organizations or CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (1) FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, (2) manufacturing standards, (3) federal and state healthcare fraud and abuse laws and regulations, or (4) laws that require the reporting of true and accurate financial information and data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic collaborators, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to commercialize AKB-9778, if approved, and any other product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, administrative and, if necessary, sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;

- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize any product candidates that we may develop; and
- a decline in our stock price.

Failure to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. We currently carry product liability insurance covering our clinical trials in the amount of $10 million in the aggregate. Although we maintain product liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Ownership of Our Common Stock

We are eligible to be treated as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company", as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions

from various reporting requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- an exemption from new or revised financial accounting standards until they would apply to private companies and not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We have taken advantage of these reduced reporting burdens. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. Investors may find our common stock less attractive if we continue to rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have total annual gross revenue of $1.07 billion (as may be inflation-adjusted by the SEC from time to time) or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.07 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" if the market value of our common stock held by non-affiliates is below $75 million as of June 30 in any given year, which would allow us to take advantage of many of the same exemptions from disclosure requirements, including exemption from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

Because we are quoted on the OTCQB instead of a national exchange or quotation system, our investors may experience significant volatility in the market price of our stock and have difficulty selling their shares.

Our common stock is currently quoted on the OTC Market Group's OTCQB Market quotation system under the ticker symbol "ARPO." The OTCQB are regulated quotation services that display real-time quotes, last sale prices and volume limitations in over-the-counter securities. Trading in shares quoted on the OTCQB is often thin and characterized by volatility in trading prices. This volatility may be caused by a variety of factors, including the lack of readily available price quotations, the absence of consistent administrative supervision of bid and ask quotations, lower trading volume and market conditions. As a result, there may be wide fluctuations in the market price of the shares of our common stock for reasons unrelated to operating performance, and this

volatility, when it occurs, may have a negative effect on the market price for our securities. Moreover, the OTCQB is not a stock exchange, and trading of securities on them is often more sporadic than the trading of securities listed on a national quotation system or stock exchange. Accordingly, our stockholders may not be able to realize a fair price from their shares when they determine to sell them or may have to hold them for a substantial period of time until the market for our common stock improves.

The designation of our common stock as a "penny stock" would limit the liquidity of our common stock.

Our common stock may be deemed a "penny stock" (as that term is defined under Rule 3a51-1 of the Exchange Act) in any market that may develop in the future. Generally, a "penny stock" is a common stock that is not listed on a securities exchange and trades for less than $5.00 a share. Prices often are not available to buyers and sellers and the market may be very limited. Penny stocks in start-up companies are among the riskiest equity investments. Broker-dealers who sell penny stocks must provide purchasers of these stocks with a standardized risk-disclosure document prepared by the SEC. The document provides information about penny stocks and the nature and level of risks involved in investing in the penny stock market. A broker must also provide purchasers with bid and offer quotations and information regarding broker and salesperson compensation and make a written determination that the penny stock is a suitable investment for the purchaser and obtain the purchaser's written agreement to the purchase. Many brokers choose not to participate in penny stock transactions. Because of the penny stock rules, there may be less trading activity in penny stocks in any market that develops for our common stock in the future and stockholders are likely to have difficulty selling their shares.

FINRA sales practice requirements may limit a stockholder's ability to buy and sell our stock.

The Financial Industry Regulatory Authority, or FINRA, has adopted rules requiring that, in recommending an investment to a customer, a broker-dealer must have reasonable grounds for believing that the investment is suitable for that customer. Prior to recommending speculative or low-priced securities to their non-institutional customers, broker-dealers must make reasonable efforts to obtain information about the customer's financial status, tax status, investment objectives and other information. Under interpretations of these rules, FINRA has indicated its belief that there is a high probability that speculative or low-priced securities will not be suitable for at least some customers. If these FINRA requirements are applicable to us or our securities, they may make it more difficult for broker-dealers to recommend that at least some of their customers buy our common stock, which may limit the ability of our stockholders to buy and sell our common stock and could have an adverse effect on the market for and price of our common stock.

The market price of our common stock may be highly volatile, and may be influenced by numerous factors, some of which are beyond our control.

If a market for our common stock develops, its market price could fluctuate substantially due to a variety of factors, including market perception of our ability to meet our growth projections and expectations, quarterly operating results of other companies in the same industry, trading volume in our common stock, changes in general conditions in the economy and the financial markets or other developments affecting our business and the business of others in our industry. In addition, the stock market itself is subject to extreme price and volume fluctuations. This volatility has had a significant effect on the market price of securities issued by many companies for reasons related and unrelated to their operating performance and could have the same effect on our common stock. The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- results of clinical trials of our product candidates;
- the timing of the release of results of our clinical trials;
- results of clinical trials of our competitors' products;
- safety issues with respect to our products or our competitors' products;

- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated fluctuations in our financial condition and operating results;
- publication of research reports by securities analysts about us or our competitors or our industry;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- the passage of legislation or other regulatory developments affecting us or our industry;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities;
- changes in market conditions for biopharmaceutical stocks; and
- changes in general market and economic conditions.

In addition, the stock market has recently experienced significant volatility, particularly with respect to pharmaceutical, biotechnology and other life sciences company stocks. The volatility of pharmaceutical, biotechnology and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. As we operate in a single industry, we are especially vulnerable to these factors to the extent that they affect our industry or our products, or to a lesser extent our markets. In the past, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

As of December 31, 2017, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 65.6% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

Because we became a reporting company under the Exchange Act by means other than a traditional underwritten initial public offering, we may not be able to attract the attention of research analysts at major brokerage firms.

Because we did not become a reporting company by conducting an underwritten initial public offering of our common stock, and because we will not be listed on a national securities exchange, security analysts of brokerage

firms may not provide coverage of our company. In addition, investment banks may be less likely to agree to underwrite secondary offerings on our behalf or recommend the purchase of our common stock than they might if we became a public reporting company by means of an underwritten initial public offering, because they may be less familiar with our company as a result of more limited coverage by analysts and the media, and because we became public at an early stage in our development. The failure to receive research coverage or support in the market for our shares will have an adverse effect on our ability to develop a liquid market for our common stock.

The resale of shares covered by a registration statement could adversely affect the market price of our common stock in the public market, should one develop, which result would in turn negatively affect our ability to raise additional equity capital.

The sale, or availability for sale, of our common stock in the public market may adversely affect the prevailing market price of our common stock and may impair our ability to raise additional capital by selling equity or equity-linked securities. We filed and caused to become effective a registration statement with the SEC registering the resale of 27,367,117 shares of our common stock issued in connection with the reverse merger and the concurrent private placement offering in March 2017. This registration statement permits the resale of these shares at any time. The resale of a substantial number of shares of our common stock in the public market could adversely affect the market price for our common stock and make it more difficult for you to sell shares of our common stock at times and prices that you feel are appropriate. Furthermore, we expect that, because there will be a large number of shares registered pursuant to a registration statement, selling stockholders will continue to offer shares covered by such registration statement for a significant period of time, the precise duration of which cannot be predicted. Accordingly, the adverse market and price pressures resulting from an offering pursuant to a registration statement may continue for an extended period of time and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital.

Issuance of stock to fund our operations may dilute your investment and reduce your equity interest.

We may need to raise capital in the future to fund the development of our drug candidates or for other purposes. Any equity financing may have significant dilutive effect to stockholders and a material decrease in our stockholders' equity interest in us. Equity financing, if obtained, could result in substantial dilution to our existing stockholders. At its sole discretion, our board of directors may issue additional securities without seeking stockholder approval, and we do not know when we will need additional capital or, if we do, whether it will be available to us.

We have broad discretion in the use of our cash and may not use them effectively.

We currently intend to use our cash resources for continuing clinical development of AKB-9778 in patients with diabetic retinopathy, including the continuation of our ongoing trials and the preparation for and initiation of the Phase 3 trials and for working capital and other general corporate purposes. Although we currently intend to use our cash resources in such a manner, we will have broad discretion in the application of such cash resources. Our failure to apply these funds effectively could affect our ability to continue to develop and commercialize our product candidates. Pending their use, we may invest our cash resources in a manner that does not produce income or loses value.

As a result of recently becoming a public company, we are incurring increased costs and our management devotes substantial time to public company compliance programs.

As a public company, we incur significant legal, insurance, accounting and other expenses that we did not incur as a private company. In addition, our administrative staff is required to perform additional tasks. We are investing resources to comply with evolving laws, regulations and standards, and this investment will result in increased general and administrative expenses and may divert management's time and attention from product

development activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed. In connection with the reverse merger, pursuant to which we acquired Aerpio, we increased our directors' and officers' insurance coverage, which increased our insurance cost. In the future, it will be more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced coverage or incur substantially higher costs to obtain coverage. These factors could also make it more difficult for us to attract and retain qualified members of our board of directors, particularly to serve on our audit committee and compensation committee, and qualified executive officers.

In addition, in order to comply with the requirements of being a public company, we may need to undertake various actions, including implementing new internal controls and procedures and hiring new accounting or internal audit staff. The Sarbanes-Oxley Act requires that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that information required to be disclosed in reports under the Securities Exchange Act of 1934 as amended, or the Exchange Act, is accumulated and communicated to our principal executive and financial officers. Any failure to develop or maintain effective controls could adversely affect the results of periodic management evaluations. In the event that we are not able to demonstrate compliance with the Sarbanes-Oxley Act, that our internal control over financial reporting is perceived as inadequate, or that we are unable to produce timely or accurate financial statements, investors may lose confidence in our operating results and the price of our ordinary shares could decline. In addition, if we are unable to continue to meet these requirements, we may not be able to obtain listing on a national securities exchange.

Our management team and board of directors will need to devote significant efforts to maintaining adequate and effective disclosure controls and procedures and internal control over financial reporting in order to comply with applicable regulations, which may include hiring additional legal, financial reporting and other finance and accounting staff and engaging consultants to assist in designing and implementing such procedures. Additionally, any of our efforts to improve our internal controls and design, implement and maintain an adequate system of disclosure controls may not be successful and will require that we expend significant cash and other resources. In addition, our management will be required to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of our internal control over financial reporting commencing with our second annual report. This assessment will need to include the disclosure of any material weaknesses in our internal control over financial reporting identified by our management or our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statement.

Our independent registered public accounting firm will not be required to formally attest to the effectiveness of our internal control over financial reporting until the later of our second annual report or the first annual report required to be filed with the SEC following the date we are no longer an "emerging growth company" as defined

in the JOBS Act. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal controls in the future.

Our independent registered public accounting firm has identified a material weakness in our internal control over financial reporting which will require remediation.

Our independent registered public accounting firm issued a letter to our audit committee and management in which they identified certain matters that they consider to constitute material weaknesses in the design and operation of our internal control over financial reporting as of December 31, 2016. A deficiency in internal control over financial reporting exists when the design or operation of a control does not allow management or employees, in the normal course of performing their assigned functions, to prevent or detect misstatements on a timely basis. A significant deficiency is a deficiency, or a combination of deficiencies, in internal control over financial reporting that is less severe than a material weakness, yet important enough to merit attention by those responsible for the oversight of the company's financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis.

The material weaknesses identified by our auditors relate to deficiencies with our disclosure controls and procedures, including review and approval procedures with respect to financial information generated to prepare our consolidated financial statements, coupled with a lack of segregation of duties as a result of our size and overall lack of resources in the accounting department. This resulted in not ensuring appropriate segregation of duties between incompatible functions, and made it more difficult to ensure review of financial reporting issues.

We are taking steps to remediate this material weakness. If we fail to remediate the material weakness, we may fail to meet our future reporting obligations, our financial statements may contain material misstatements and our operational results may be harmed. Any such failure could also adversely affect the results of the periodic management evaluations and, to the extent we are no longer an emerging growth company, the annual auditor attestation reports regarding the effectiveness of our internal control over financial reporting that will be required under Section 404 of the Sarbanes-Oxley Act of 2002. Internal control deficiencies could also cause investors to lose confidence in our reported financial information.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated by-laws may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a majority of the directors then in office;
- prohibit stockholder action by written consent;

- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- prohibit the consummation of a liquidation event unless approved by a supermajority (66 2/3% and majority of the minority, if applicable) vote of the holders of our voting stock;
- prohibit the consummation of an affiliate transaction with a majority stockholder that holds more than 50% of the voting power of our capital stock unless approved by a supermajority (66 2/3%) vote of directors then in office;
- provide that the number of directors on our board of directors may only be changed with a supermajority (66 2/3%) of directors then in office, even though less than a quorum;
- provide that our directors may be removed only for cause and by a supermajority (66 2/3%) vote of the holders of our voting stock;
- provide that vacancies on our board of directors may be filled only by a supermajority (66 2/3%) of directors then in office, even though less than a quorum;
- require a supermajority (66 2/3% and majority of the minority, if applicable) vote of the holders of our voting stock or the supermajority (66 2/3%) vote of the members of our board of directors then in office to amend our amended and restated by-laws; and
- require a supermajority (66 2/3% and majority of the minority, if applicable) vote of the holders of our voting stock and a supermajority (66 2/3%) vote of the holders of each class of our voting stock entitled to vote thereon to amend certain provisions of our amended and restated certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated by-laws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our ability to use net operating losses to offset future taxable income may be subject to certain limitations.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, to offset future taxable income. Our existing NOLs may be subject to substantial limitations arising from previous ownership changes, and if we undergo an ownership change in connection with our private placement offering, our ability to utilize NOLs could be further limited by Section 382 of the Code. Future analysis will still be required on any historical NOLs. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Section 382 of the Code. Our NOLs may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs. Furthermore, our ability to utilize our NOLs is conditioned upon our attaining profitability and generating U.S. federal taxable income. As described above under “—Risks related to our financial position and need for

additional capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; thus, we do not know whether or when we will generate the U.S. federal taxable income necessary to utilize our NOLs. A full valuation allowance has been provided for the entire amount of our NOLs.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our operations. In addition, any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “could,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “potential,” “continue,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section “Risk Factors.”

This prospectus contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our research and development programs and future preclinical and clinical studies;
- our ability to advance any product candidates into, and successfully complete, clinical studies and obtain regulatory approval for them;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization, marketing and manufacturing of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- the implementation of our strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;
- our expectations related to the use of our existing cash resources, and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations;
- our financial performance;
- developments relating to our competitors and our industry, including the impact of government regulation; and
- other risk and uncertainties, including those listed under the caption “Risk Factors” in this prospectus and any prospectus supplement that we may file.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties and other factors more fully discussed in the “Risk Factors” section in this prospectus, the section of any accompanying prospectus supplement entitled “Risk Factors” and the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under “Item 1A. Risk Factors” and elsewhere in our Quarterly Reports on Form 10-Q for the quarters ended September 30, 2017, June 30, 2017 and March 31, 2017, and our Current Reports on Form 8-K.

Given these uncertainties, readers should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake to update any forward-looking statements after the date of this prospectus or the respective dates of documents incorporated by reference herein or therein that include forward-looking statements.

PROSPECTUS SUMMARY

The following summary highlights selected information contained elsewhere in this prospectus. This summary is not complete and does not contain all the information that should be considered before investing in our securities. Before making an investment decision, investors should carefully read the entire prospectus, paying particular attention to the risks referred to under the headings "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" and our financial statements and the notes to those financial statements.

Overview

Aerpio is a biopharmaceutical company focused on advancing first-in-class treatments for ocular disease. Our lead product candidate, AKB-9778, a small molecule activator of the Tie2 pathway, is being developed for the treatment of diabetic retinopathy, or DR, a disease characterized by progressive compromise of blood vessels in the back of the eye. The Tie2 receptor is expressed almost exclusively in endothelial cells (cells that make up blood vessels) and is essential for regulating vascular stability and preventing blood vessel compromise associated with diabetes. We have completed a Phase 2a trial of AKB-9778 in 144 patients with diabetic eye disease. Based on the results from this trial, we believe AKB-9778 has the potential to reverse the damage to blood vessels caused by diabetes. In contrast to marketed treatments for DR that are administered by a physician via intraocular injection, we intend to deliver AKB-9778 systemically by self-administered subcutaneous injection, similar to insulin. We believe that this delivery method provides an opportunity to treat diabetic eye disease at an earlier stage and reduces the likelihood of developing vision-threatening complications. In June 2017, we initiated a 48-week, double-masked, Phase 2b clinical trial, which we refer to as TIME-2b, in patients with DR who have not developed more serious complications such as diabetic macular edema, or DME or proliferative diabetic retinopathy, or PDR.

According to the World Health Organization's Global Report of Diabetes, there are an estimated 422 million individuals living with diabetes worldwide. An estimated 34.6% of these individuals, or 146 million people, have DR, 6.81%, or 28 million, have DME and 6.96%, or 29.7 million, have PDR. The underlying problem in diabetic complications is damage to the blood vessels, commonly referred to as diabetic vasculopathy, which is caused by chronic hyperglycemia. This damage causes blood vessels to leak fluid and proteins into the surrounding tissue, leading to complications. In the eyes, this damage leads to DR which can progress to DME and/or PDR. In other parts of the body such as the kidney, the damage leads to diabetic nephropathy and in the lower extremities, the damage leads to non-healing foot ulcers, peripheral artery disease and critical limb ischemia. These diabetic complications lead to life- and sight-threatening conditions including kidney dialysis, amputations and blindness that are costly to treat. Diabetic patients with complications are estimated to cost the health care system 3.5 times more than patients without complications. For example, dialysis patients cost an average of $89,000 per year and the cost for the first year of DME therapy with Eylea® is $14,400 per eye based on published Medicare allowable charges per dose and the frequency of dosing as approved by the FDA. If approved, we believe that systemic treatment with AKB-9778 could have the potential to change the treatment paradigm for diabetics in the future and potentially address a major societal problem by lowering the cost of care associated generally with diabetes.

Diabetic eye disease is one of the most common and debilitating complications of diabetes. Over time, diabetes damages blood vessels in the back of the eye. When this happens, a patient is said to have DR. Eventually, these damaged blood vessels can leak blood proteins and fluid into the central portion of the retina, called the macula, which is responsible for high resolution central vision. The leakage of protein and fluid into the macula causes swelling, a condition called DME. The more progressive stages of DR, referred to as PDR, are characterized by the growth of abnormal new blood vessels. These new blood vessels can bleed into the eye and if left untreated can result in decreased visual acuity and eventual blindness. The likelihood of a person developing these sight-threatening complications increases as DR progresses.

According to the 2017 revenue reports for Regeneron and Roche, sales of the two leading approved therapies for DME, Eylea (aflibercept), which is marketed by Regeneron and Lucentis (ranibizumab), which is marketed by Genentech and Novartis, were estimated to be over $5.6 billion worldwide in 2017. Given that the number of patients with DR is roughly five times that for DME, we believe that a therapy that can reverse early ocular damage in patients with DR and slow or prevent the development of DME or PDR, without requiring repeated injections into the eye, could have substantial clinical and commercial value.

AKB-9778 is a small molecule activator of the Tie2 pathway that we believe helps to stabilize blood vessel walls and prevent vascular compromise in the eye, and based on pre-clinical models, potentially elsewhere in the body. Such vascular compromise in the eye may eventually lead to DME or PDR and, in many cases, to loss of vision or even blindness. We believe AKB-9778's mechanism of action reduces vascular damage and restores vascular integrity. In contrast to current therapies for diabetic eye disease, which are all administered by a physician via repeated injections into the eye, AKB-9778 is being developed as a self-administered subcutaneous injection that allows for treatment of both eyes.

In addition to DR, the Tie2 pathway is also implicated in other diabetic complications. We believe systemic treatment with AKB-9778 may address diabetic nephropathy and peripheral vascular disease. If we are successful in developing and commercializing AKB-9778 for DR, we intend to conduct longer term clinical trials to evaluate AKB-9778's potential to reduce or delay the need for kidney dialysis and reduce amputations.

The TIME-2b study is a double-masked, placebo-controlled multi-center trial that is currently ongoing and has enrolled 167 patients randomized evenly to receive either AKB-9778 15 mg subcutaneously once daily, AKB-9778 15 mg subcutaneously twice daily or placebo for a 48-week treatment period. The primary endpoint of the TIME-2b study is the percentage of patients who improve by 2 or more steps in DR Severity Score, or DRSS, in the study eye.

There is emerging scientific literature that supports the role of Tie 2 in the maintenance of conventional outflow, or CO, pathway in the front of the eye. Existing preclinical and clinical evidence suggest the potential of AKB-9778 for reducing intraocular pressure in primary open angle glaucoma, or POAG, and ocular hypertension. We plan to initiate a Phase 1b clinical trial in the first quarter of 2019 to evaluate AKB-9778 for POAG and, if we observe positive results, we expect to initiate a Phase 2 program for this indication.

We are also developing AKB-4924, a selective stabilizer of hypoxia-inducible factor-1 alpha, or HIF-1 alpha, that is being developed for the treatment of inflammatory bowel disease. HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. We have completed a single ascending dose clinical trial in healthy volunteers for AKB-4924 and plan to initiate a multiple ascending dose, or MAD study in the second quarter of 2018. If we successfully complete the MAD study, we expect to initiate a Phase 1b clinical study of AKB-4924 in patients with ulcerative colitis in the second half of 2018.

ARP-1536, our humanized monoclonal antibody directed at the same target as AKB-9778, is in preclinical development. We are evaluating development options for ARP-1536, including once-monthly subcutaneous injection for the treatment of diabetic vascular complications and once-monthly intravitreal injection for the treatment of advanced diabetic eye disease such as DME or PDR.

Our Strategy

Our objective is to become the leader in the treatment of diabetic eye disease. We are taking the following critical steps to achieve this goal:

- Advance the development of AKB-9778 for DR;
- If approved for DR, establish collaborations to commercialize AKB-9778 globally;

- Investigate the potential of AKB-9778 in other indications; and
- Advance or partner our pipeline programs AKB-4924 and ARP-1536.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus. These risks include the following:

- we have incurred significant losses since inception and anticipate that we will continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability;
- we will require substantial additional financing. A failure to obtain this necessary capital when needed could force us to delay, limit, reduce or terminate our product development or commercialization efforts;
- we depend heavily on the success of one product candidate, AKB-9778, which is in Phase 2 clinical development. Even if we obtain favorable clinical results, we may not be able to obtain regulatory approval for, or successfully commercialize, AKB-9778;
- we have not obtained agreement with the FDA, EMA or other regulatory authorities on the design of our Phase 3 development program;
- clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from Phase 1 and Phase 2a clinical trials of AKB-9778 are not necessarily predictive of the results of our completed and any future clinical trials of AKB-9778. If we cannot replicate the positive results from our Phase 1 and Phase 2a clinical trials of AKB-9778 in our ongoing and subsequent clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize AKB-9778;
- we may experience delays in our ongoing Phase 2b clinical trial for AKB-9778 and we do not know whether ongoing or planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all;
- we rely on third parties to conduct preclinical studies and clinical trials for our product candidates, and if they do not properly and successfully perform their obligations to us, we may not be able to obtain regulatory approvals for our product candidates;
- we may not be successful in establishing and maintaining strategic collaborations, which could adversely affect our ability to develop and commercialize our product candidates, negatively impacting our operating results;
- if our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market;
- our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and others in the medical community;
- our independent registered public accounting firm has identified a material weakness in our internal control over financial reporting which will require remediation; and
- our shareholders will have limited ability to influence corporate matters because a small number of our existing shareholders hold a significant amount of our outstanding common stock.

Reverse Merger and Private Placement Offering

We were incorporated as Zeta Acquisition Corp. II in the State of Delaware on November 16, 2007. Prior to the Merger (as defined below), we were a "shell company" (as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended).

On March 15, 2017, we changed our name to Aerpio Pharmaceuticals, Inc. by filing a Certificate of Amendment to our Certificate of Incorporation. On March 3, 2017, our board of directors, and on March 10, 2017, our pre-Merger (as defined below) stockholders, approved an amended and restated certificate of incorporation, which, among other things, increased our authorized capital stock from 100,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share, to 300,000,000 shares of common stock, par value $0.0001 per share and 10,000,000 shares of preferred stock, par value $0.0001 per share. Our amended and restated certificate of incorporation was made effective upon its filing with the Secretary of State of the State of Delaware on April 17, 2017. On March 15, 2017, our board of directors adopted the amended and restated bylaws.

On March 15, 2017, our wholly-owned subsidiary, Aerpio Acquisition Corp., a corporation formed in the State of Delaware on March 3, 2017, or the Acquisition Sub, merged with and into Aerpio Therapeutics, Inc., a corporation incorporated on November 17, 2011 in the State of Delaware referred to herein as Aerpio. Pursuant to this transaction, or the Merger, Aerpio was the surviving corporation and became our wholly-owned subsidiary. All of the outstanding capital stock of Aerpio was converted into shares of our common stock on a 2.3336572:1 basis, as described in more detail below.

As a result of the Merger, we acquired the business of Aerpio and will continue the existing business operations of Aerpio as a public reporting company under the name Aerpio Pharmaceuticals, Inc. Immediately after the effective time of the Merger, on March 15, 2017, Aerpio converted into a Delaware limited liability company by the filing of a Certificate of Conversion with the Secretary of State of the State of Delaware, which we refer to as the Conversion.

Immediately following the Conversion, the pre-Merger stockholders of Zeta Acquisition Corp. II surrendered for cancellation 4,000,000 of the 5,000,000 shares of the outstanding common stock of Zeta Acquisition Corp. II. We refer to these transactions as the Share Cancellation. Following the Share Cancellation, on March 15, 2017, we closed a private placement offering, or the Offering, of 8,049,555 shares of our common stock, at a purchase price of $5.00 per share.

Unless otherwise indicated in this prospectus, all share and per share figures reflect the exchange of each 2.3336572 shares of Aerpio common stock then outstanding for 1 share of our common stock at the effective time of the Merger; however, the share and per share numbers in the audited financial statements of Aerpio for the year ended December 31, 2016 included in this prospectus are not adjusted to give effect to the Merger.

The issuance of shares of our common stock in the Merger and in the Offering was exempt from registration under Section 4(a)(2) of the Securities Act of 1933, as amended, or the Securities Act, and Regulation D promulgated thereunder.

Company Information

We were originally incorporated in the State of Delaware in November 2007 under the name “Zeta Acquisition Corp. II.” Prior to the Merger, Zeta Acquisition Corp. II was a “shell” company registered under the Exchange Act with no specific business plan or purpose until it began operating the business of Aerpio through the Merger transaction on March 15, 2017. Aerpio was incorporated in the State of Delaware in November 2011 to focus primarily on advancing first-in-class treatments for ocular disease. Effective upon the Merger, a wholly-owned subsidiary of Zeta Acquisition Corp. II merged with and into Aerpio, and Aerpio continued as the operating subsidiary of Zeta Acquisition Corp. II. Immediately following the Merger, Aerpio converted into a Delaware limited liability company with the name Aerpio Therapeutics LLC.

Our corporate headquarters are located at 9987 Carver Road, Cincinnati, Ohio 45242, and our telephone number is (513) 985-1920. We maintain a website at www.aerpio.com, to which we regularly post copies of our press

releases as well as additional information about us. Our filings with the Securities and Exchange Commission, or SEC, will be available free of charge through the website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this prospectus or our other filings with the SEC.

All brand names or trademarks appearing in this prospectus are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this prospectus is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- an exemption from new or revised financial accounting standards until they would apply to private companies and from compliance with any new requirements adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenue of $1.07 billion or more; (ii) December 31, 2022; (iii) the date on which we have issued more than $1.07 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC. We may choose to take advantage of some but not all of these exemptions. We have irrevocably elected to "opt out" of the exemption for the delayed adoption of certain accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

SUMMARY FINANCIAL DATA

The following tables summarize Aerpio's financial data for the periods presented and should be read together with the sections of this prospectus entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," and our financial statements and related notes appearing elsewhere in this prospectus. The summary financial data in this section are not intended to replace our financial statements and related notes. The following summary consolidated financial data for the years ended December 31, 2016 and 2015 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The summary consolidated financial data as of September 30, 2017 and for the nine months ended September 30, 2017 and 2016 have been derived from our unaudited consolidated financial statements included elsewhere in this prospectus. In our opinion, these unaudited financial statements have been prepared on a basis consistent with our audited consolidated financial statements and contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such consolidated financial data. Our historical results are not necessarily indicative of our future results, and our operating results for the nine-month period ended September 30, 2017 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2017 or any other interim periods or any future year or period.

	Nine months ended September 30,		Year Ended December 31,	
	2017	2016	2016	2015
	(unaudited)			
Statement of Operations data:				
Operating expenses:				
Research and development	$ 8,366,869	$ 9,374,383	$ 11,367,590	$ 11,625,404
General and administrative	6,732,816	3,953,808	5,265,995	5,861,151
Total operating expenses	15,099,685	13,328,191	16,633,585	17,486,555
Loss from operations	(15,099,685)	(13,328,191)	(16,633,585)	(17,486,555)
Grant income	93,720	116,185	131,281	369,688
Interest income (expense), net	(159,612)	(254,552)	(482,204)	19,622
Other income, net	—	997	997	27,022
Total other income (expense)	(65,892)	(137,370)	(349,926)	416,332
Net and comprehensive loss	$ (15,165,577)	$ (13,465,561)	$ (16,983,511)	$ (17,070,223)
Reconciliation of net loss attributable to common stockholders:				
Net and comprehensive loss	$ (15,165,577)	$ (13,465,561)	$ (16,983,511)	$ (17,070,223)
Extinguishment of preferred stock	—	224,224	—	224,224
Accretion of redeemable convertible preferred stock to redemption value	(943,297)	(3,098,149)	(3,928,577)	(572,660)
Net loss attributable to common stockholders	$ (16,108,874)	$ (16,339,486)	$ (20,912,088)	$ (17,418,659)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.81)	$ (20.01)	$ (24.52)	$ (31.14)
Weighted average number of common shares used in computing net loss per share attributable to common stockholders, basic and diluted	19,889,984	816,395	852,665	559,419

	September 30, 2017	December 31, 2016	December 31, 2015
		(unaudited)	
Balance Sheet data:			
Cash and cash equivalents	$ 24,828,910	$ 1,609,694	$ 5,144,211
Total assets	26,001,610	2,396,878	6,092,534
Working capital, net	(23,277,544)	(12,631,294)	3,805,729
Redeemable convertible preferred stock	—	73,757,890	70,487,415
Accumulated deficit	(102,327,627)	(86,218,753)	(66,554,870)
Total stockholders' equity (deficit)	23,415,377	(86,218,629)	(66,554,755)

RATIO OF EARNINGS TO FIXED CHARGES

Our earnings were insufficient to cover fixed charges for each of the periods in the table below, and we are unable to disclose a ratio of earnings to fixed charges for such periods. The table below sets forth our deficiency of earnings to cover fixed charges on a historical basis for the periods indicated. You should read this table in conjunction with the financial statements and notes incorporated by reference in this prospectus. The table is qualified by the more detailed information appearing in the computation table found in Exhibit 12.1 to the registration statement of which this prospectus is a part.

	Nine Months Ended September 30, 2017	Year Ended December 31, 2016	Year Ended December 31, 2015
		(in thousands)	
Deficiency of Earnings to Fixed Charges	$ (4,896)	$ (17,466)	$ (17,070)

Earnings consist of loss from operations before the benefit from income taxes and fixed charges. Fixed charges consist of the sum of interest expenses and the component of rental expenses that we believe to be representative of the interest factor for these amounts.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include costs to commercialize our products, research and development and clinical development costs to support the advancement of our product candidates and the expansion of our product candidate pipeline; funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or may hold such proceeds as cash, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

PRICE RANGE OF COMMON STOCK

Our common stock trades on the OTC Markets—OTCQB Tier under the symbol “ARPO.” The following table sets forth the high and low bid information for the common stock for each quarterly period in the most recent fiscal year as reported on the OTCQB marketplace:

	High	Low
2017		
Quarter ended September 30, 2017	$6.75	5.90
Quarter ended December 31, 2017	6.60	4.00
Period ended February 16, 2018	5.25	4.28

On February 16, 2018, the last reported sale price for our common stock on the OTCQB marketplace was $4.50 per share. As of January 31, 2018, there were 258 holders of record of the common stock.

DIVIDEND POLICY

We have never paid any cash dividends on our capital stock and do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain future earnings to fund ongoing operations and future capital requirements. Any future determination to pay cash dividends will be at the discretion of our board of directors and will be dependent upon financial condition, results of operations, capital requirements and such other factors as the board of directors deems relevant.

DILUTION

We will set forth in a prospectus supplement the following information regarding any material dilution of the equity interests of investors purchasing securities in an offering under this prospectus:

- the net tangible book value per share of our equity securities before and after the offering;
- the amount of the increase in such net tangible book value per share attributable to the cash payments made by purchasers in the offering; and
- the amount of the immediate dilution from the public offering price which will be absorbed by such purchasers.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with the "Summary Financial Data" and our consolidated financial statements included elsewhere in this prospectus.

Operating Overview

We are a biopharmaceutical company focused on advancing first-in-class treatments for ocular disease. Our lead product candidate, AKB-9778, a small molecule activator of the Tie-2 pathway, is being developed for the treatment of diabetic retinopathy, or DR, a disease characterized by progressive compromise of blood vessels in the back of the eye. The Tie2 receptor is expressed almost exclusively in endothelial cells (cells that make up blood vessels) and is essential for regulating vascular stability and preventing blood vessel compromise associated with diabetes. We have completed a Phase 2a trial of AKB-9778 in 144 patients with diabetic eye disease. Based on the results from this trial, we believe AKB-9778 has the potential to reverse the damage to blood vessels caused by diabetes. In contrast to marketed treatments for DR that are administered by a physician via intraocular injection, we intend to deliver AKB-9778 systemically by self-administered subcutaneous injection, similar to insulin. We believe that this delivery method provides an opportunity to treat diabetic eye disease at an earlier stage and reduces the likelihood of developing vision-threatening complications. In June 2017, we initiated a 48-week, double-masked, Phase 2b clinical trial, which we refer to as TIME-2b, in patients with DR who have not developed more serious complications such as diabetic macular edema, or DME or proliferative diabetic retinopathy, or PDR.

The TIME-2b study is a double-masked, placebo-controlled multi-center trial that is currently on-going and has enrolled 167 patients randomized evenly to receive either AKB-9778 15 mg subcutaneously once daily, AKB-9778 15 mg subcutaneously twice daily or placebo for a 48-week treatment period. The primary endpoint of the TIME-2b study is the percentage of patients who improve by at least 2 steps in DR Severity Score, or DRSS in the study eye.

We are also developing AKB-4924, a selective stabilizer of hypoxia-inducible factor-1 alpha, or HIF-1 alpha, that is being developed for the treatment of inflammatory bowel disease. HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. We have completed a single ascending dose clinical trial in healthy volunteers for AKB-4924 and plan to initiate a multiple ascending dose, or MAD study in the second quarter of 2018. If we successfully complete the MAD study, we expect to initiate a Phase 1b clinical study of AKB-4924 in patients with ulcerative colitis in the second half of 2018.

ARP-1536, our humanized monoclonal antibody directed at the same target as AKB-9778, is in preclinical development. We are evaluating development options for ARP-1536, including once-monthly subcutaneous injection for the treatment of diabetic vascular complications and once-monthly intravitreal injection for the treatment of advanced diabetic eye disease such as DME or PDR.

Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates, and undertaking preclinical and clinical studies. We have not generated any revenues to date, nor is there any assurance of future revenues. Our product candidates are subject to long development cycles, and there is no assurance we will be able to successfully develop, obtain regulatory approval for, or market our product candidates. As of September 30, 2017, we had an accumulated deficit of $102.3 million and anticipate incurring additional losses for the next several years.

Our primary source of liquidity to date has been through the private placement offering of our common stock (the "Offering") in March 2017 and the historical sales of redeemable convertible preferred stock, common stock and proceeds from convertible debt. The aggregate net proceeds from the Offering in March 2017 was $37.2 million.

In 2016, we raised a total of $12.5 million through the issuance of secured convertible notes. In 2017, we raised a total of $0.3 million through the issuance of secured convertible notes. In 2014, we raised a total of $22.0 million ($21.8 million net of offering costs) through the issuance of redeemable convertible preferred stock. We will need to raise additional funds to further advance our clinical research programs, commence additional clinical trials, and commercialize our products, if approved. While we continue to pursue financing alternatives, which may include equity financing, business development arrangements, licensing arrangements and business combination transactions, financing may not be available to us in the necessary time frame, in the amounts that we need, on terms that are acceptable to us or at all. If we are unable to raise the necessary funds when needed or reduce spending on currently planned activities, we may not be able to continue the development of our product candidates or we could be required to delay, scale back, or eliminate some or all of our development programs and other operations and will materially harm our business and consolidated financial position.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We expect our expenses will increase substantially in connection with our ongoing activities, as we:

- continue our research and development efforts, primarily in connection with our ongoing TIME-2b clinical trial;
- add personnel to support our clinical development program; and
- operate as a public company.

We are subject to a number of risks similar to other life science companies in the current stage of our life cycle, including, but not limited to, the need to obtain adequate additional funding, possible failure of preclinical testing or clinical trials, competitors developing new technological innovations, and protection of proprietary technology. If we do not successfully mitigate any of these risks, we will be unable to generate revenue or achieve profitability. The condensed consolidated accompanying financial statements have been prepared assuming our Company will continue as a going concern, which contemplates the realization of assets and payments of liabilities in the ordinary course of business. We had cash and cash equivalents and short-term investments of $24.8 million at September 30, 2017. We believe our existing cash and cash equivalents and short-term investments, will be sufficient to fund currently planned operations into the fourth quarter of fiscal year 2018.

Basis of Presentation

The unaudited interim condensed consolidated financial statements of the Company for the three months ended September 30, 2017 and 2016, and the nine months ended September 30, 2017 and 2016, contained herein, include a summary of our significant accounting policies and should be read in conjunction with the discussion below.

Other Recent Developments

Listing on the OTCQB Market

Shares of our common stock were approved for trading and began trading on August 8, 2017 on the OTCQB marketplace under the symbol “ARPO.”

Merger

On March 15, 2017, our wholly-owned subsidiary, Aerpio Acquisition Corp., a corporation formed in the State of Delaware, or the Acquisition Sub, merged with and into Aerpio Therapeutics, Inc., (“Aerpio”) a corporation incorporated on November 17, 2011, under the laws of the State of Delaware. Pursuant to this transaction, or the Merger, Aerpio was the surviving corporation and became our wholly-owned subsidiary. We changed our name from Zeta Acquisition Corp II to Aerpio Pharmaceuticals, Inc. All the outstanding stock of Aerpio was converted into shares of our common stock.

At the effective time of the Merger, the legal existence of Acquisition Sub ceased and each 2.3336572 shares of Aerpio common and preferred stock that was issued and outstanding immediately prior to the effective time of the Merger, including share based awards, whether vested or unvested issued under the Aerpio Therapeutics, Inc. 2011 Equity Incentive Plan (the "2011 Plan"), was automatically exchanged for one share of our common stock. In addition, immediately prior to the Merger, the outstanding amounts under certain senior secured convertible notes issued by Aerpio to its pre-Merger noteholders were converted into Aerpio common stock, which were converted in the Merger into shares of our common stock at the same ratio. We issued an aggregate of 18,000,000 shares of our common stock upon such exchange of the outstanding shares of Aerpio common stock. In addition, at the effective time of the Merger, we assumed Aerpio's 2011 Equity Incentive Plan. At the effective time of the Merger, we assumed the outstanding options under the 2011 Plan and converted them into options to purchase 927,592 shares of our common stock. As a result of the Merger, we acquired the business of Aerpio and will continue the existing business operations of Aerpio as a public reporting company under the name Aerpio Pharmaceuticals, Inc. Immediately after the Merger, Aerpio was converted into a Delaware limited liability company (the "Conversion").

The Merger was treated as a recapitalization and reverse acquisition for financial reporting purposes. We are the legal acquirer of Aerpio in the transaction. However, Aerpio is considered the acquiring company for accounting purposes since (i) former Aerpio stockholders own in excess of 50% of the combined enterprise on a fully diluted basis immediately following the Merger and Offering, and (ii) all members of the Company's executive management and Board of Directors are from Aerpio. In accordance with the "reverse merger" or "reverse acquisition" accounting treatment, the unaudited condensed consolidated interim financial statements for the period ended September 30, 2017 include the accounts of the Company and its wholly owned subsidiary, Aerpio Therapeutics, LLC. The comparative historical financial statements for periods ended prior to the date of the Merger are the historical financial statements of Aerpio.

The following discussion highlights Aerpio's results of operations and the principal factors that have affected our financial condition as well as our liquidity and capital resources for the periods described, and provides information that management believes is relevant for an assessment and understanding of the unaudited condensed consolidated statements of financial condition and results of operations presented herein. The following discussion and analysis are based on the Company's unaudited condensed consolidated financial statements contained in this Quarterly Report on Form 10-Q, which we have prepared in accordance with United States generally accepted accounting principles. You should read the discussion and analysis together with such condensed consolidated financial statements and the related notes thereto.

Share Cancellation

Following the Merger and Conversion, and immediately prior to the closing of the Offering, an aggregate of 4,000,000 of the 5,000,000 shares of our common stock that were held by the pre-Merger stockholders of Zeta Acquisition Corp. II were surrendered for cancellation (the "Share Cancellation").

Offering

Following the Merger, the Conversion and the Share Cancellation, we sold to accredited investors $40.2 million of our shares of common stock, or 8,049,555 shares, at a price of $5.00 per share, (net proceeds of $37.2 million after deducting placement agent fees and expenses of the offering). In connection with the Offering, we issued warrants to purchase 317,562 shares of our common stock at $5.00 per share to the placement agents for the Offering. The warrants are exercisable for three years. The Offering closed on March 15, 2017.

Components of Statements of Operations and Comprehensive Loss

Operating Expenses

Research and Development. Research and development expenses consist primarily of compensation and related costs for personnel, including stock-based compensation, employee benefits and travel. These costs also consist

of third-party service providers for our potential product development activities, third-party consulting services, laboratory supplies, research materials, medical equipment, computer equipment, and related depreciation and amortization. We expense research and development expenses as incurred. As we continue to invest in basic research and clinical development of our product candidates, we expect research and development expenses to increase in absolute dollars.

General and Administrative. Our general and administrative expenses consist primarily of compensation and related costs for personnel, including stock-based compensation, employee benefits and travel, for our finance, human resources and other administrative personnel. In addition, general and administrative expenses include third-party consulting, legal, patent, audit, accounting services, and facilities costs. We expect general and administrative expenses to increase in absolute dollars following the consummation of the Merger due to additional legal, accounting, insurance, investor relations and other costs associated with being a public company, as well as other costs associated with growing our business.

Interest Income (Expense), Net

Interest income consists primarily of interest income received on our cash and cash equivalents. Interest expense consists primarily of interest and amortization of debt issuance costs related to our secured convertible promissory notes issued in 2016 and 2017. The secured convertible notes have converted into shares of our common stock in connection with the Merger and Offering.

Grant Income

Grant income is recognized as earned based on contract work performed.

Results of Operations

The following tables set forth our results of operations for the periods presented:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Operating expenses:				
Research and development	$ 2,942,170	$ 3,481,261	$ 8,366,869	$ 9,374,383
General and administrative	1,814,068	1,264,054	6,732,816	3,953,808
Total operating expenses	4,756,238	4,745,315	15,099,685	13,328,191
Loss from operations	(4,756,238)	(4,745,315)	(15,099,685)	(13,328,191)
Grant income	46,824	26,561	93,720	116,185
Interest income (expense), net	59,847	(166,847)	(159,612)	(254,552)
Other income, net	—	—	—	997
Total other income (expense)	106,671	(140,286)	(65,892)	(137,370)
Net and comprehensive loss	$ (4,649,567)	$ (4,885,601)	$ (15,165,577)	$ (13,465,561)

Comparison of the Three Months Ended September 30, 2017 and 2016

Operating Expenses

	Three Months Ended September 30,	
	2017	2016
Operating expenses:		
Research and development	$ 2,942,170	$ 3,481,261
General and administrative	1,814,068	1,264,054
Total operating expenses	$ 4,756,238	$ 4,745,315

Research and Development

Research and development expenses for the three months ended September 30, 2017, decreased approximately $0.5 million or 15%, compared to the three months ended September 30, 2016. This decrease was the result of decreased spending on our pipeline programs—AKB-4924 and ARP-1536, partially offset by an increase in spending on our lead program AKB-9778.

The $0.4 million increase in spending in our lead program, AKB-9778, for the three months ended September 30, 2017 from the corresponding period in 2016 is primarily attributed to the cost of drug product, associated with our double-blind Phase 2 DR clinical trial initiated in the second quarter of 2017, partially offset by a decrease in pre-clinical and Phase 1 clinical trial expenses incurred in the prior period.

The $0.9 million decrease in spending on our pipeline programs, for the three months ended September 30, 2017 from the corresponding period in 2016 is primarily due to our decision to focus on the lead program while pursuing alternative strategies to fund further development activities for one or both the pipeline programs. Healthy volunteers were enrolled in the AKB-4924 Phase 1a clinical trial and cell line development expenses were incurred on ARP-1536 during the 2016 period.

General and Administrative.

General and administrative expenses in the three months ended September 30, 2017, increased $0.6 million, or 44%, compared to the three months ended September 30, 2016. This increase was primarily attributable to personnel and related expenses, including costs to recruit additional resources as well as professional services, including legal, accounting, insurance and other professional service expenses associated with the Merger, related transactions and operating as a public company.

Other Income (Expense) net

	Three Months Ended September 30,	
	2017	2016
Other income (expense):		
Grant income	$ 46,824	$ 26,561
Interest income (expense), net	59,847	(166,847)
Total other income (expense), net	$106,671	$(140,286)

Grant income

Grant income is recognized as earned based on contract work performed. Grant income amounts can vary greatly from period to period depending on the funding and needs of the party for whom we perform the requested services.

Interest income (expense), net

Interest income in the three months ended September 30, 2017, reflects interest earned during the period on cash balances invested in short term money market instruments. The net proceeds received in the Offering on March 15, 2017, less cash used in operations, were available for investment. The interest expense in the corresponding three-month period in 2016, was primarily related to the senior secured convertible notes issued in April 2016, offset in part by a small amount of interest income earned on invested cash balances. We completed three note financings in fiscal 2016 totaling an aggregate principal amount of approximately $12.5 million and one note financing in the first quarter of fiscal 2017, totaling an aggregate principal amount of approximately $0.3 million. The financings were funded in four tranches', beginning with one in April 2016 for $4.5 million, one in July 2016 for $4.5 million, one in October 2016 for $3.5 million and one in January 2017 for $0.3 million. The notes accrued interest at the rate of eight percent (8%) per annum, compounded annually. The principal and accrued interest on the secured convertible notes was converted into common stock on March 15, 2017, in connection with the Merger.

Comparison of the Nine Months Ended September 30, 2017 and 2016

Operating Expenses

	Nine Months Ended September 30,	
	2017	2016
Operating expenses:		
Research and development	$ 8,366,869	$ 9,374,383
General and administrative	6,732,816	3,953,808
Total operating expenses	$ 15,099,685	$ 13,328,191

Research and Development

Research and development expenses for the nine months ended September 30, 2017, decreased approximately $1.0 million, or 11%, compared to the nine months ended September 30, 2016. This decrease was the result of decreased spending on our pipeline programs AKB-4924 and ARP-1536, partially offset by an increase in spending on our lead program AKB-9778, currently in Phase 2b development.

The approximate $1.0 million increase in spending on our lead program, AKB-9778, for the nine months ended September 30, 2017 from the corresponding period in 2016 is primarily attributed to the cost of drug product for our double-blind Phase 2 DR clinical trial initiated during the second quarter of 2017, partially offset by a decrease in pre-clinical and Phase 1 clinical trial expenses incurred in the prior period.

The approximate $2.0 million decrease in spending on our pipeline programs, for the nine months ended September 30, 2017 from the corresponding period in 2016 is primarily due to our decision to focus on the lead program while pursuing alternative strategies to fund further development activities for one or both the pipeline programs. During the nine months ended September 30, 2016, healthy volunteers were enrolled in the AKB-4924 Phase 1a clinical trial and cell line development expenses were incurred on ARP-1536.

General and Administrative

General and administrative expenses in the nine months ended September 30, 2017, increased $2.8 million, or 70%, compared to the nine months ended September 30, 2016. This increase was primarily attributable to personnel and related expenses, including costs to recruit additional resources as well as professional services including, legal, accounting, insurance and other professional service expenses associated with the Merger, related transactions and operating as a public company.

Other expense, net

	Nine Months Ended September 30,	
	2017	2016
Other (expense) income:		
Grant income	$ 93,720	$ 116,185
Interest expense, net	(159,612)	(254,552)
Other income, net	—	997
Total other expense, net	$ (65,892)	$(137,370)

Grant income

Grant income is recognized as earned based on contract work performed. Grant income amounts can vary greatly from period to period depending on the funding and needs of the party for whom we perform the requested services.

Interest expense, net

Interest expense in the nine months ended September 30, 2017, was primarily related to the senior secured convertible notes issued in 2016 and 2017, offset by interest income earned during the period on cash balances invested in short term money market instruments. The net proceeds received in the Offering on March 15, 2017, less cash used in operations during the period, were available for investment. The interest expense in the corresponding nine-month period in 2016, was primarily related to the senior secured convertible notes issued in April 2016, offset in part by a small amount of interest income earned on invested cash balances. We completed three note financings in fiscal 2016 totaling an aggregate principal amount of approximately $12.5 million and one note financing in the first quarter of fiscal 2017, totaling an aggregate principal amount of approximately $0.3 million. The convertible note financings were funded in four tranches', beginning with one in April 2016 for $4.5 million, one in July 2016 for $4.5 million, one in October 2016 for $3.5 million and one in January 2017 for $0.3 million. The notes had interest at the rate of eight percent (8%) per annum, compounded annually. The principal and accrued interest on the secured convertible notes was converted into common stock on March 15, 2017, in connection with the Merger.

Other income

Other income represents amounts received from Akebia for services rendered under the shared services agreements. The agreements expired in 2016.

Liquidity and Capital Resources

Since inception, we have incurred significant net losses and negative cash flows from operations. For the three months ended September 30, 2017 and 2016, we had net losses of $4.6 million and $4.9 million, respectively. At September 30, 2017 and December 31, 2016, we had an accumulated deficit of $102.3 million and $86.2 million, respectively.

At September 30, 2017, we had cash and cash equivalents and short-term investments of $24.8 million. To date, we have financed our operations principally through the Offering, private placements of our redeemable convertible preferred stock, common stock and issuances of secured convertible promissory notes. Based on our current plans**,** we expect that our existing cash and cash equivalents, will enable us to conduct our planned operations into the fourth quarter of fiscal 2018.

We could potentially use our available financial resources sooner than we currently expect, and we may incur additional indebtedness to meet future operation liquidity. We continuously evaluate our needs for additional

capital and consider opportunities on an ongoing basis, including capital from many different sources including equity capital, strategic alliances, business development debt, collaborations and business combinations. Adequate additional funding may not be available to us on acceptable terms or at all. In addition, although we anticipate being able to obtain additional financing through non-dilutive means, we may be unable to do so. Our failure to raise capital as and when needed could have significant negative consequences for our business, financial condition and results of operations. Our future capital requirements and the adequacy of available funds will depend on many factors, including those set forth in the section titled "Risk Factors."

The following table summarizes our cash flows for the periods presented:

	Nine Months Ended September 30,	
	2017	2016
Net cash used in operating activities	$(14,271,082)	$(12,676,283)
Net cash used in investing activities	(6,547)	(113,297)
Net cash provided by financing activities	37,496,845	8,953,719
Net increase (decrease) in cash and cash equivalents	$ 23,219,216	$ (3,835,861)

Operating Activities

We have historically experienced negative cash outflows as we developed AKB-9778, ARP-1536 and AKB-4924. Our net cash used in operating activities primarily results from our net loss adjusted for non-cash expenses and changes in working capital components. Our primary uses of cash from operating activities are amounts due to contract research organizations for the conduct of our clinical programs and employee-related expenditures for research and development, and general and administrative activities. Our cash flows from operating activities will continue to be affected principally by increased spending to advance of our product candidates in the clinic, personnel to support those activities and other operating and general administrative activities.

For the nine months ended September 30, 2017, operating activities used approximately $14.3 million in cash, primarily as a result of our net loss of approximately $15.2 million, offset by approximately $0.7 million in non-cash charges that consisted primarily of stock compensation expense, non-cash interest expense, amortization of debt issuance costs and depreciation expense and approximately $0.2 million from changes in working capital. For the nine months ended September 30, 2016, operating activities used approximately $12.7 million in cash, primarily as a result of our net loss of $13.5 million, offset by approximately $0.8 million of non-cash charges of stock compensation expense, non-cash interest expense, amortization of debt issuance costs and depreciation expense.

Investing Activities

Cash used in investing activities for both nine month periods ended September 30, 2017 and 2016 was due to capital expenditures to support our operations. In addition, in the nine months ended September 30, 2016, we acquired approximately $0.1 million of laboratory equipment to support internal drug development capabilities.

Financing Activities

During the nine months ended September 30, 2017, we received net proceeds of $37.5 million from the sale of common stock at $5.00 per share, issued in the Offering and $0.3 million in January from an extension to the Aerpio senior secured convertible notes. During the nine months ended September 30, 2016, we received $8.9 million from the issuance of and an extension to the Aerpio senior secured convertible notes.

On March 31, 2016, Aerpio entered into a senior secured convertible note financing with certain preferred stock investors of Aerpio. The secured convertible notes accrued interest at 8% per annum, compounded annually.

Each of the secured convertible notes were also subject to mandatory prepayment and were also convertible into preferred stock of Aerpio upon the occurrence of certain events, as described in the Note Agreements.

We received proceeds from the first tranche in April 2016 and subsequent tranches in July 2016, October 2016 and January 2017. The outstanding principal and accrued interest under the secured convertible notes was converted into shares of Aerpio common stock immediately prior to the effective time of the Merger, and exchanged for shares of our common stock pursuant to the Merger.

Contractual Obligations and Commitments

There have been no material changes outside the ordinary course of business during the three months ended September 30, 2017, from the contractual obligations and commitments as of December 31, 2016.

Off-Balance Sheet Arrangements

As of September 30, 2017 and 2016, we did not have any off-balance sheet arrangements as defined by applicable SEC regulations.

Critical Accounting Policies and Estimates

Our condensed consolidated financial statements are prepared in accordance with U.S. generally accepted accounting principles or GAAP. The preparation of these condensed consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and related disclosures. We evaluate our estimates and assumptions on an ongoing basis. Our estimates are based on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Our actual results could differ from these estimates.

We believe that the assumptions and estimates have the greatest potential impact on our condensed consolidated financial statements. Therefore, we consider these to be our critical accounting policies and estimates. For further information on all our significant accounting policies, see the notes to our financial statements.

Prepaid and Accrued Research and Development Expenses

As part of the process of preparing our condensed consolidated financial statements, we are required to estimate our prepaid and accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our prepaid and accrued research and development expenses as of each condensed consolidated balance sheet date in our financial statements based on facts and circumstances known to us at the time. We confirm the accuracy of estimates with the service providers and make adjustments if necessary. Examples of estimated prepaid and accrued research and development expenses include expenses for:

- Clinical Research Organizations (CROs) in connection with clinical studies;
- Investigative sites in connection with clinical studies;
- Vendors in connection with preclinical development activities; and
- Vendors related to product manufacturing, development and distribution of clinical materials.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical studies on our behalf. The financial

terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. The scope of services under these contracts can be modified and some of the agreements may be cancelled by either party upon written notice. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical study milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates and the amount actually incurred.

Stock-Based Compensation

We issue stock-based awards generally in the form of stock options and restricted stock. We account for our stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock and modifications to existing stock awards to be recognized in the statements of operations and comprehensive loss based on their fair values. Described below is the methodology we have utilized in measuring stock-based compensation expense.

We estimate the fair value of our options to purchase shares of common stock to employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of the expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to our company, including stage of product development and life science industry focus. We are a development stage company in an early stage of product development with no revenues and the representative group of companies has certain similar characteristics. We believe the group selected has sufficient similar economic and industry characteristics, and includes companies that are most representative of our Company. We use the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted to employees and non-employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The expected term is applied to the stock option grant group as a whole, as we do not expect substantially different exercise or post-vesting termination behavior among our employee population. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock, similar to our peer group. The grant date fair value of restricted stock award grants is based on the estimated value of our common stock at the date of grant.

Our stock-based awards are subject to service-based vesting conditions. Compensation expense related to awards to employees with service-based vesting conditions is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, which is generally the vesting term. Awards to non-employees are adjusted through share-based compensation expense as the award vests to reflect the current fair value of such awards and are expensed using an accelerated attribution model.

During the three months ended September 30, 2017 and 2016, and the nine months ended September 30, 2017 and 2016 stock-based compensation expense was approximately $0.1 million, $0.1 million, $0.4 million and

$0.4 million, respectively. As of September 30, 2017, we had $0.2 million of total unrecognized stock-based compensation costs for stock options, which we expect to recognize over a weighted-average period of 2.0 years. As of September 30, 2017, we had $0.2 million of total unrecognized stock-based compensation costs for restricted stock awards, which we expect to recognize over a weighted-average period of 1.2 years.

Common Stock Valuations

The fair value of the common stock was determined by our Board of Directors, which intended all stock options granted to be exercisable at a price per share not less than the per share fair value of our common stock underlying those options on the date of grant. In 2016, as a privately held company, the valuations of our common stock were determined in accordance with the guidelines outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation* of *Privately-Held-Company Equity Securities Issued as Compensation*, or AICPA Practice Aid. The assumptions we used in the valuation model were based on future expectations combined with management judgment. In the absence of a public trading market, our board of directors, with input from management, exercised significant judgment and considered numerous objective and subjective factors to determine the fair value of our common stock as of the date of each option grant. including the following factors:

- valuations performed by unrelated third-party specialists;
- the prices, rights, preferences, and privileges of our convertible preferred stock relative to those of our common stock;
- the prices of Aerpio's former convertible preferred stock sold to outside investors in arm's-length transactions;
- the lack of marketability of our common stock;
- our actual operating and financial performance;
- current business conditions and projections;
- our hiring of key personnel and the experience of our management;
- our stage of development;
- the likelihood of achieving a liquidity event, such as a public offering or a merger or acquisition of our business given prevailing market conditions;
- the illiquidity of stock-based awards involving securities in a private company;
- the market performance of comparable publicly traded companies; and
- the U.S. and global capital market conditions.

For the valuation of our common stock at December 31, 2016, we used the hybrid method. As described in the AICPA's accounting and valuation guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, the hybrid method is a hybrid between the probability-weighted expected returns method (PWERM) and the option-pricing method (OPM). We considered a "go-public scenario", in which our preferred shares convert to common stock, and a second scenario, in which equity value is allocated using the OPM. We used the guideline public company method under the market approach to value our equity. We estimated our equity value based on a multiple of paid-in capital as indicated by a group of guideline public companies. The group consisted of clinical-stage drug development companies which completed initial public offerings in the six months preceding our appraisal date. In addition, for each of the guideline companies, we considered the increase, or step-up, in per share value from the preferred financing preceding the public offering to the common stock value in the public offering. We also considered the equity value of each guideline company, not including the proceeds of the public offering.

The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceed the value of the preferred liquidation preference at the time of a liquidity event, such as a strategic sale, merger or initial public offering. For each Black-Scholes calculation in the OPM, the option "strike price" is determined by the company's capital structure. Additional inputs to the OPM include the estimated time to liquidity and estimated equity volatility.

We applied a discount for lack of marketability to the values indicated for the common stock in the go-public and OPM scenarios. Our estimate of the appropriate discount for lack of marketability relied on an Asian put option calculation.

The following table summarizes the significant assumptions used in the hybrid method to determine the fair value of our common stock as of December 31, 2016:

	Go-Public Scenario	OPM
Key assumptions		
Probability weighting	50%	50%
Years to liquidity	0.2	2.8
Weighted-average cost of equity	25%	—
Annual volatility	—	61%
Risk-free interest rate	—	1.4%
Discount for lack of marketability (DLOM)	5%	23%

Based on these assumptions, we estimated the fair value of our common stock on a pre-Merger basis to be $1.20 as of December 31, 2016 ($2.80 as of December 31, 2016, on an as converted basis to reflect the effect of the Merger).

There are significant judgments and estimates inherent in the determination of these valuations. These judgments and estimates include assumptions regarding our future performance, including the successful enrollment and completion of our clinical studies as well as the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense could have been different. The foregoing valuation methodologies are not the only methodologies available and they will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our common stock. Accordingly, we caution you not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

For the valuation of our common stock at March 31, 2017 and June 30, 2017, we used $5.00 per share, which is the share price paid by outside investors in our private placement closed on March 15, 2017 and at September 30, 2017 we used $6.00 per share, the closing share price on the OTCQB marketplace on that date. There were no stock awards granted or issued in the nine months ended September 30, 2017.

JOBS Act Accounting Election

We are an "emerging growth company" within the meaning of the JOBS Act. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies that are not emerging growth companies.

BUSINESS

Overview

Aerpio is a biopharmaceutical company focused on advancing first-in-class treatments for ocular disease. Our lead product candidate, AKB-9778, a small molecule activator of the Tie2 pathway, is being developed for the treatment of diabetic retinopathy, or DR, a disease characterized by progressive compromise of blood vessels in the back of the eye. The Tie2 receptor is expressed almost exclusively in endothelial cells (cells that make up blood vessels) and is essential for regulating vascular stability and preventing blood vessel compromise associated with diabetes. We have completed a Phase 2a trial of AKB-9778 in 144 patients with diabetic eye disease. Based on the results from this trial, we believe AKB-9778 has the potential to reverse the damage to blood vessels caused by diabetes. In contrast to marketed treatments for DR that are administered by a physician via intraocular injection, we intend to deliver AKB-9778 systemically by self-administered subcutaneous injection, similar to insulin. We believe that this delivery method provides an opportunity to treat diabetic eye disease at an earlier stage and reduces the likelihood of developing vision-threatening complications. In June 2017, we initiated a 48-week, double-masked, Phase 2b clinical trial, which we refer to as TIME-2b, in patients with DR who have not developed more serious complications such as diabetic macular edema, or DME or proliferative diabetic retinopathy, or PDR.

According to the World Health Organization's Global Report of Diabetes, there are an estimated 422 million individuals living with diabetes worldwide. An estimated 34.6% of these individuals, or 146 million people, have DR, 6.81%, or 28 million, have DME and 6.96%, or 29.7 million, have PDR. The underlying problem in diabetic complications is damage to the blood vessels, commonly referred to as diabetic vasculopathy, which is caused by chronic hyperglycemia. This damage causes blood vessels to leak fluid and proteins into the surrounding tissue, leading to complications. In the eyes, this damage leads to DR which can progress to DME and/or PDR. In other parts of the body such as the kidney, the damage leads to diabetic nephropathy and in the lower extremities, the damage leads to non-healing foot ulcers, peripheral artery disease and critical limb ischemia. These diabetic complications lead to life- and sight-threatening conditions including kidney dialysis, amputations and blindness that are costly to treat. Diabetic patients with complications are estimated to cost the health care system 3.5 times more than patients without complications. For example, dialysis patients cost an average of $89,000 per year and the cost for the first year of DME therapy with Eylea® is $14,400 per eye based on published Medicare allowable charges per dose and the frequency of dosing as approved by the FDA. If approved, we believe that systemic treatment with AKB-9778 could have the potential to change the treatment paradigm for diabetics in the future and potentially address a major societal problem by lowering the cost of care associated generally with diabetes.

Diabetic eye disease is one of the most common and debilitating complications of diabetes. Over time, diabetes damages blood vessels in the back of the eye. When this happens, a patient is said to have DR. Eventually, these damaged blood vessels can leak blood proteins and fluid into the central portion of the retina, called the macula, which is responsible for high resolution central vision. The leakage of protein and fluid into the macula causes swelling, a condition called DME. The more progressive stages of DR, referred to as PDR, are characterized by the growth of abnormal new blood vessels. These new blood vessels can bleed into the eye and if left untreated can result in decreased visual acuity and eventual blindness. The likelihood of a person developing these sight-threatening complications increases as DR progresses.

According to the 2017 revenue reports for Regeneron and Roche, sales of the two leading approved therapies for DME, Eylea (aflibercept), which is marketed by Regeneron and Lucentis (ranibizumab), which is marketed by Genentech and Novartis, were estimated to be over $5.6 billion worldwide in 2017. Given that the number of patients with DR is roughly five times that for DME, we believe that a therapy that can reverse early ocular damage in patients with DR and slow or prevent the development of DME or PDR, without requiring repeated injections into the eye, could have substantial clinical and commercial value.

AKB-9778 is a small molecule activator of the Tie2 pathway that we believe helps to stabilize blood vessel walls and prevent vascular compromise in the eye, and based on pre-clinical models, potentially elsewhere in the body.

Such vascular compromise in the eye may eventually lead to DME or PDR and, in many cases, to loss of vision or even blindness. We believe AKB-9778's mechanism of action reduces vascular damage and restores vascular integrity. In contrast to current therapies for diabetic eye disease, which are all administered by a physician via repeated injections into the eye, AKB-9778 is being developed as a self-administered subcutaneous injection that allows for treatment of both eyes.

In addition to DR, the Tie2 pathway is also implicated in other diabetic complications. We believe systemic treatment with AKB-9778 may address diabetic nephropathy and peripheral vascular disease. If we are successful in developing and commercializing AKB-9778 for DR, we intend to conduct longer term clinical trials to evaluate AKB-9778's potential to reduce or delay the need for kidney dialysis and reduce amputations.

The TIME-2b study is a double-masked, placebo-controlled multi-center trial that is currently ongoing and is now fully enrolled with 167 patients randomized evenly to receive either AKB-9778 15 mg subcutaneously once daily, AKB-9778 15 mg subcutaneously twice daily or placebo for a 48-week treatment period. The primary endpoint of the TIME-2b study is the percentage of patients who improve by 2 or more steps in DR Severity Score, or DRSS, in the study eye.

There is emerging scientific literature that supports the role of Tie 2 in the maintenance of conventional outflow, or CO, pathway in the front of the eye. Existing preclinical and clinical evidence suggest the potential of AKB-9778 for reducing intraocular pressure in primary open angle glaucoma, or POAG, and ocular hypertension. We plan to initiate a Phase 1b clinical trial in the first quarter of 2019 to evaluate AKB-9778 for POAG and, if we observe positive results, we expect to initiate a Phase 2 program for this indication.

We are also developing AKB-4924, a selective stabilizer of hypoxia-inducible factor-1 alpha, or HIF-1 alpha, that is being developed for the treatment of inflammatory bowel disease. HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. We have completed a single ascending dose clinical trial in healthy volunteers for AKB-4924 and plan to initiate a multiple ascending dose, or MAD study in the second quarter of 2018. If we successfully complete the MAD study, we expect to initiate a Phase 1b clinical study of AKB-4924 in patients with ulcerative colitis in the second half of 2018.

ARP-1536, our humanized monoclonal antibody directed at the same target as AKB-9778, is in preclinical development. We are evaluating development options for ARP-1536, including once-monthly subcutaneous injection for the treatment of diabetic vascular complications and once-monthly intravitreal injection for the treatment of advanced diabetic eye disease such as DME or PDR.

Our Strategy

Our objective is to become the leader in the development of Tie2-targeted therapeutics for the treatment of vascular disorders. We are taking the following critical steps to achieve this goal:

- **Advance the development of AKB-9778 for diabetic retinopathy**

In June 2017, we initiated a 48-week, double-masked, Phase 2b clinical trial, TIME-2b, in patients with DR who have not developed more serious complications such as DME or PDR. We expect to report topline data in the second quarter of 2019.

- **If approved for DR, establish collaborations to commercialize AKB-9778 globally**

If approved, we intend to independently pursue the approval and commercialization of AKB-9778 for DR in the U.S. We believe that many health care providers, including general ophthalmologists, endocrinologists, and primary care physicians have the potential to treat early diabetic eye disease with AKB-9778, and we plan on utilizing a multi-faceted strategy that will engage these various health care providers. Outside of the U.S., we intend to pursue the approval and commercialization of AKB-9778 for DR through strategic collaborations. We

may develop and commercialize AKB-9778 for other indications independently or through collaborations with third parties.

- **Advance the development of AKB-9778 for primary open angle glaucoma**

We plan to evaluate a topical formulation of AKB-9778 for POAG into a proof-of-concept Phase 1b study in the first quarter of 2019. If we observe positive results from this study, we expect to initiate a Phase 2 program to evaluate AKB-9778 for POAG.

- **Investigate the potential of AKB-9778 in other indications**

The downregulation of Tie2 occurs in the vasculature of diabetics systemically, particularly in the kidney. While we are initially focused on the development of AKB-9778 for DR, our ongoing Phase 2b trial includes exploratory endpoints to study the effects of AKB-9778 on diabetic kidney disease. If we observe positive signals in these exploratory endpoints, we intend to explore clinical development of AKB-9778 in diabetic nephropathy.

- **Advance AKB-4924 in inflammatory bowel disease**

We plan to advance the development of AKB-4924 in inflammatory bowel disease. We plan to initiate a MAD study in healthy volunteers in the second quarter of 2018. If we successfully complete the MAD study, we plan to initiate a Phase 1b study in patients with ulcerative colitis in the second half of 2018.

- **Advance the development of ARP-1536**

We are currently evaluating development options for ARP-1536. We are evaluating development options for ARP-1536, including once-monthly subcutaneous injection for the treatment of diabetic vascular complications and once-monthly intravitreal injection for advanced diabetic eye disease (DME/PDR).

AKB-9778 for diabetic retinopathy

We believe that AKB-9778, if approved, has the potential to be a market leader for the treatment of early stage diabetic eye disease, DR that has not yet developed vision-threatening complications. There are currently approximately 100 million individuals globally with DR, and this number is projected to continue to grow over the next 30 years. AKB-9778 is designed to eliminate intraocular injections, reduce physician visit burden, simultaneously treat both eyes, of which an estimated65-70% of diabetic eye disease patients have bilateral disease, reduce or slow progression to development of vision-threatening events, such as DME and PDR, and protect other vascular beds affected by diabetes.

We have completed a Phase 2a trial of AKB-9778 in 144 patients with diabetic retinopathy complicated by diabetic macular edema. We observed the following results in this trial:

- We observed promising signs of reduction in the severity of diabetic retinopathy when AKB-9778 was used as monotherapy.
- These improvements in diabetic retinopathy severity were seen bilaterally, in the study and fellow eye.
- AKB-9778 monotherapy had fewer ocular and non-ocular adverse events than either Lucentis (ranibizumab) monotherapy or combination therapy.

Diabetic Retinopathy Overview

DR is a frequent complication of diabetes and is a leading cause of visual impairment and blindness among working-age individuals. Patients with DR have a progressive compromise of microvasculature which eventually manifests as leaky blood vessels that allow fluid and blood to leak into surrounding tissues. This leakage presents problems in areas of the body that are highly vascularized such as the retina and the kidney. Fluid leakage in the

eye can distort vision directly and the loss of blood flow to other parts of the retina can result in local oxygen deprivation or hypoxia. This hypoxia then triggers the formation of new blood vessels; however, these new vessels are often not well-formed and leaky, leading to further deterioration of vision. In some cases, there is excessive accumulation of fluid or edema near the center of the retina or macula that has severe effects on vision. This accumulation is referred to as DME. This edema leads to thickening of the macula region of the retina and loss of visual acuity. The various features of DR vascular dysfunction are illustrated in the following graphic.

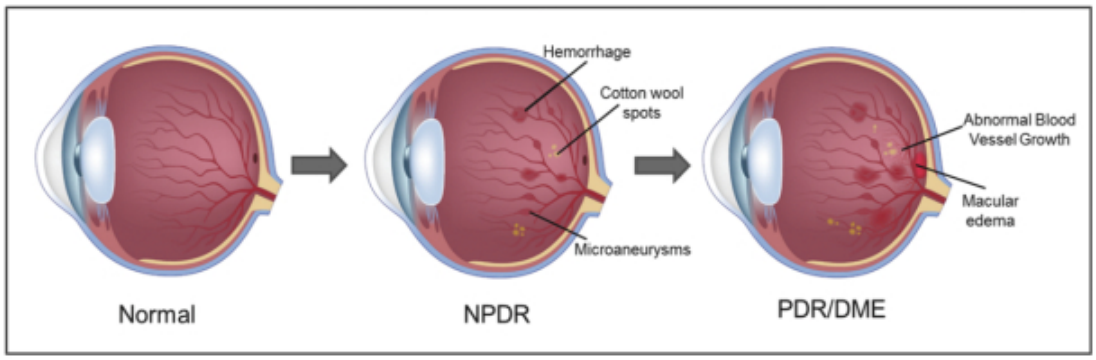

Figure 1: Progression of diabetic eye disease is characterized by worsening vascular compromise.

The severity of DR is evaluated using the Early Treatment Diabetic Retinopathy Study, or ETDRS, severity scale. This scale is divided into 11-discreet steps with less severe disease having lower step scores and more advanced disease having higher step scores. The natural history of DR in most patients is a progressive worsening that can be captured in photographs of the retina, shown below. In its initial stages, DR is characterized by vascular changes in the retina that are detectable by color photography of the back of the eye, or fundus. In these early stages, visual function can remain intact even in the presence of profound vascular compromise. The progression of DR severity is associated with increased risk for vision loss due to the growth of abnormal blood vessels, typical in DME and PDR.

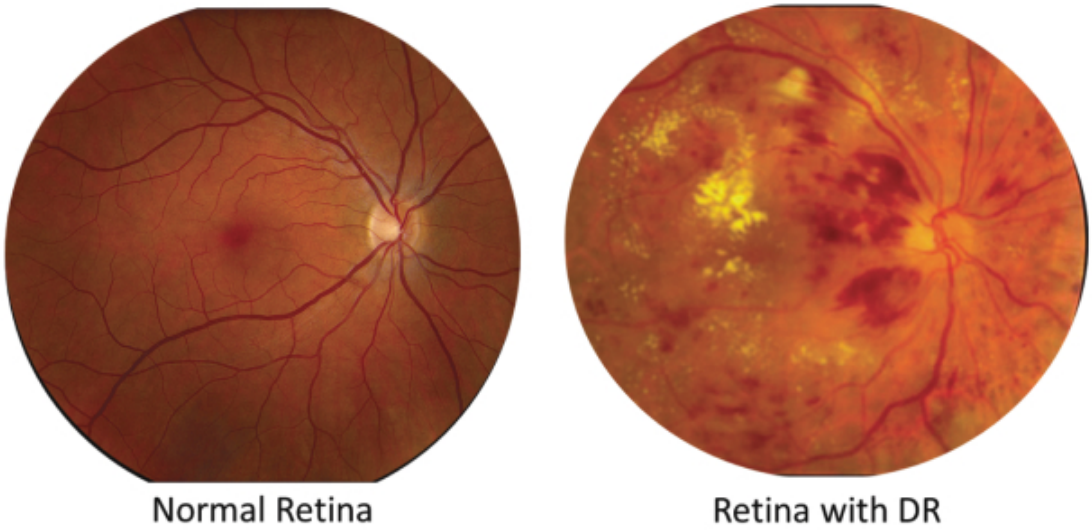

Figure 2. Fundus photographs or a normal retina (left) and a retina with advanced DR (right)

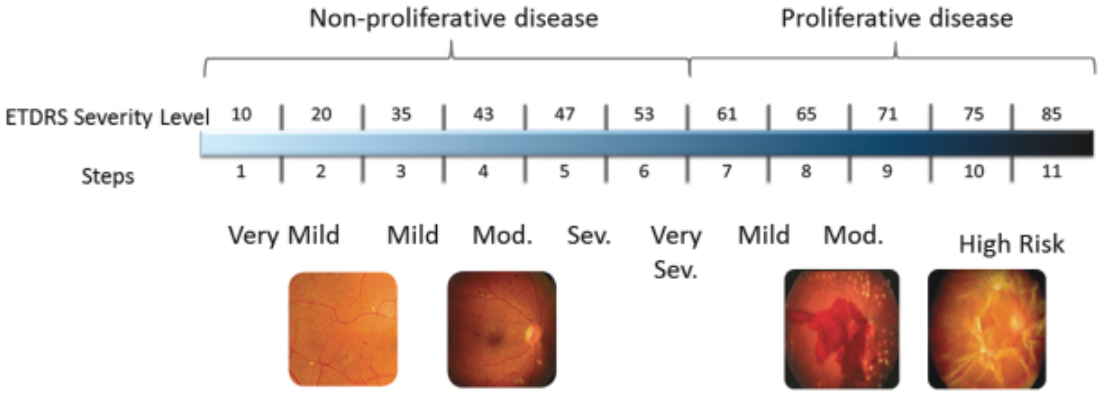

Figure 3: Early Treatment of Diabetic Retinopathy Study scale used to grade fundus images of the retina and measure the progression and regression of diabetic retinopathy.

The majority of diabetic patients will eventually develop DR. By 20 years after disease diagnosis, nearly 100% of type 1 diabetics and 60% of type 2 diabetics will have developed DR. Among an estimated 19.8 million US adults forty years and older known to have diabetes (Types 1 and 2), prevalence rates for DR and DME were 23.7% (4.7 million) and 3.8% (746,000), respectively. We believe both DR and DME are likely to persist as public health problems due to both the aging of the global population and increasing prevalence of diabetes over time.

Current Treatments for DR

Laser photocoagulation is sometimes used to treat DR prior to the development of vision-threatening events. This treatment entails using a high-energy laser to destroy diseased retinal tissue and cauterize leaking blood vessels. While this therapy prevents further vision loss, it does not address the pathology of constant and prolonged vascular damage that happens in the diabetic retina, and is therefore not considered a disease-modifying therapy. In addition to destroying retinal tissue, laser photocoagulation can be associated with several adverse events including transient decreases in central vision, black spots in the center or around the center of a patient's vision, delayed or impaired adaption of vision in dark settings, visual field defects or proliferation of abnormal blood vessels leading to macular edema

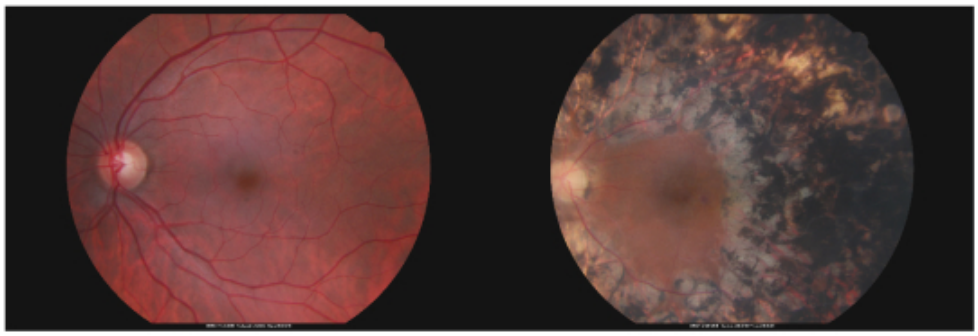

Figure 4: Normal retina (left). Retina after panretinal laser photocoagulation (right).

Lucentis was recently approved for the treatment of diabetic retinopathy. This approval was based on the ability of monthly intraocular injections of Lucentis to improve underlying diabetic retinopathy by two or more steps on

the ETDRS scale compared to placebo at the end of one year of treatment. However, Lucentis requires intraocular injections and monthly visits to the ophthalmologist which could create patient burden and discomfort. Furthermore, if the patient presents with bilateral disease, the patient must undergo separate intraocular injections in each eye.

If we are successful in developing and obtaining approval of AKB-9778 for the treatment of DR we believe that we can be market leaders in the space due to the potential advantages of AKB-9778, including the potential to eliminate intraocular injections, reduce physician visit burden, simultaneously treat both eyes, of which approximately65-70% of diabetic eye disease patients have bilateral disease, reduce or slow progression to development of vision-threatening events, such as DME and PDR, and protect other vascular beds affected by diabetes.

Role of Tie2 in Diabetic Disease

Tie2 is a receptor that is normally activated in healthy blood vessels. When active, Tie2 is a key regulator of vascular stability and function. In its active state, Tie2 maintains blood vessel stability by several mechanisms, including tightening the junctions between the cells that line blood vessels, maintaining support cell coverage of blood vessels, and resisting growth signaling from proliferative cytokines. In diabetic patients, an upregulation of vascular endothelial protein tyrosine phosphatase, or VE-PTP, an enzyme that inactivates Tie2, leads to vascular destabilization.

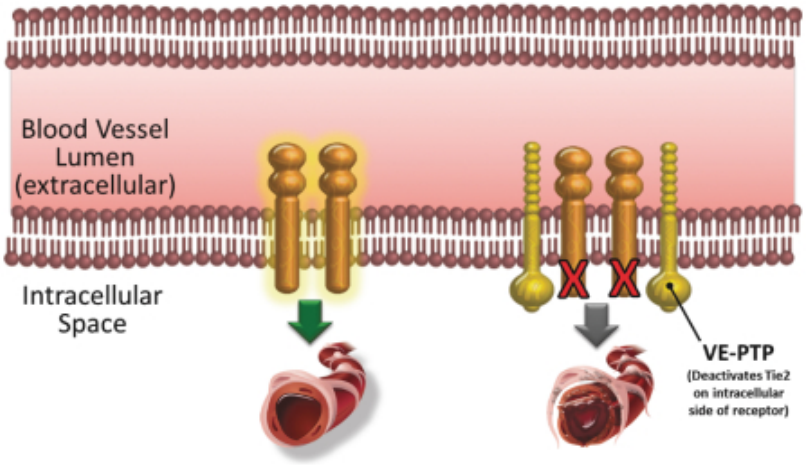

Figure 5. VE-PTP is upregulated in diabetic vasculature and leads to deactivation of the Tie2 receptor

Our Solution AKB-9778

AKB-9778 works by inhibiting VE-PTP, an enzyme that is upregulated in diabetic eye disease and that is responsible for inactivating Tie2. AKB-9778 was developed using modern drug discovery techniques such as structure-based drug design to selectively target and inhibit VE-PTP at sub-nanomolar concentrations and has a

high degree of selectivity. The potency and selectivity of AKB-9778 minimize the potential for off-target side effects. Inhibition of the inhibitor, VE-PTP, by AKB-9778 leads to activation of Tie2.

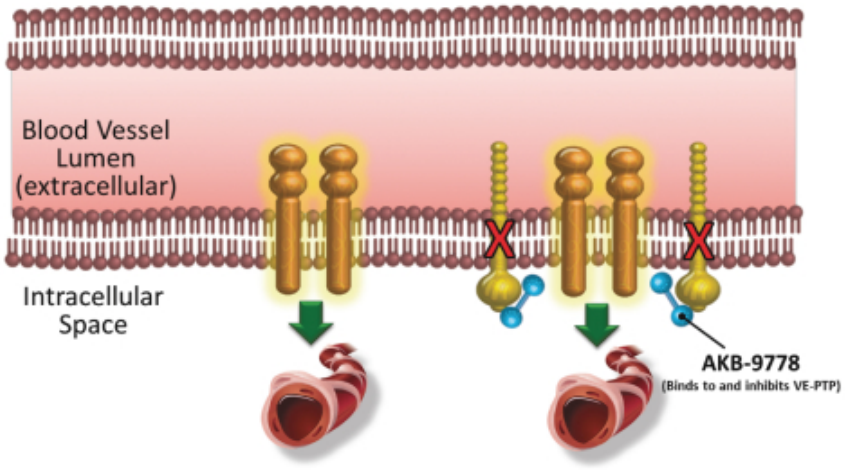

Figure 6. AKB-9778 binds to and inhibits the active site of VE-PTP, resulting in Tie2 activation.

We believe that AKB-9778 may hold a competitive advantage versus other product candidates that are currently in development that target other aspects of the Tie2 pathway. We are aware that two other companies, Roche and Regeneron, are developing agents that inhibit Ang-2, a natural antagonist of Tie2. Ang-2 can bind to Tie2 and prevent Ang-1 dependent activation. However, simply reducing the levels of Ang-2 has no effect on the activity of VE-PTP, which inactivates Tie2 further downstream of Ang-2 binding. Direct inhibition of the inhibitor, VE-PTP, has a larger effect on Tie2 activation than elimination of Ang-2.

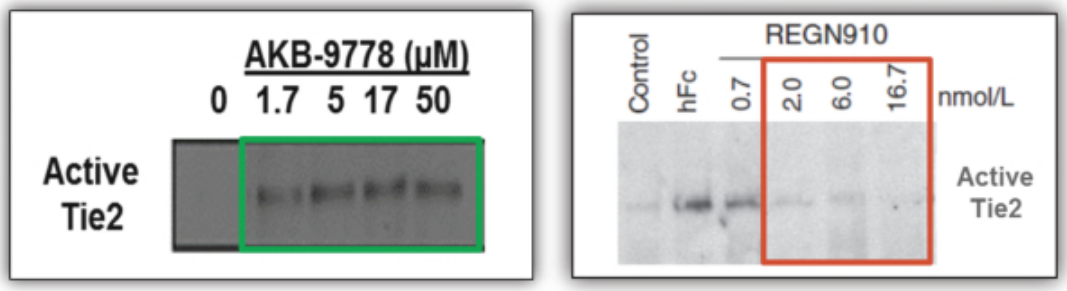

Figure 7. Inhibiting VE-PTP with AKB-9778 robustly activates Tie2 in human endothelial cells in pre-clinical experiments (Shen et al. JCI 124:4564-76, 2014). Ang-2 inhibition, with REGN910 (nesvacumab), results in minimal Tie2 activation in human endothelial cells in pre-clinical experiments (Daly et al. Cancer Research 73:108-18, 2012.).

Clinical Results in DME

We completed a double-masked Phase 2a trial in 144 patients with AKB-9778 in DME. In this trial 15 mg of AKB-9778 was administered by subcutaneous injection twice daily (BID) for three months either as monotherapy or in combination with intravitreal injections of Lucentis. Patients were randomized to receive subcutaneous AKB-9778 + sham intravitreal injections, subcutaneous AKB-9778 + Lucentis intravitreal

injections, or subcutaneous placebo + Lucentis intravitreal injections. Only one eye, designated as the study eye, received the intravitreal injections. In addition to efficacy measures based on parameters related to DME, the efficacy of these agents on DR severity was also pre-defined.

Efficacy in DME was evaluated by measuring the thickness of the macula using a standard criterion called central subfield thickness, or CST. As edema, or fluid leak from blood vessels increases, the macula layer becomes distended, and rather than having a normal thickness of less than 300 µm, the DME patients in this trial had an average CST of approximately 500 µm. The reduction in retinal thickness was measured using optical coherence tomography or OCT, an imaging technology providing high resolution images showing changes in retinal thickness.

In our completed Phase 2a study the cohort of patients treated with the combination of AKB-9778 and Lucentis showed a significantly greater reduction in macular edema (mean reduction = 164.4 µm) compared to that achieved by Lucentis monotherapy (mean reduction = 110.4 µm; with p=0.008, ANCOVA using baseline values as covariate). The mean CST at end of treatment was 340.0 µm with 29.2% of eyes achieving a CST less than 300 µm in the AKB-9778 combination group versus 392.1 µm with 17.0% of eyes achieving a CST less than 300 µm in the Lucentis monotherapy group. The improvement in CST when AKB-9778 was used in combination increased between the second and third months of treatment. Based on this pattern, we believe that longer treatments with the combination of AKB-9778 and Lucentis have the potential to further reduce CST. AKB-9778 monotherapy did not show efficacy in reducing macular edema. The long standing DME in the TIME-2 study, duration of DME roughly 5 years, is characterized by large VEGF loads. Anti-VEGF therapy is required to reduce the VEGF load and the resultant permeability. In animal models, we observed that concurrent therapy with AKB-9778 activates the Tie2 receptor and normalizes vasculature in the back of the retina improving blood flow and oxygenation and reducing the stimulation of VEGF. Therefore, combination therapy may produce greater clinical activity than anti-VEGF alone and provides a hypothesis as to why Tie2 therapy alone has minimal benefit as it relates to VEGF-driven vascular permeability. In earlier disease, where vascular compromise has not progressed far enough to stimulate a VEGF response, we believe AKB-9778 may be able to positively remodel vasculature and reverse early diabetic eye disease delaying or preventing the onset of DME.

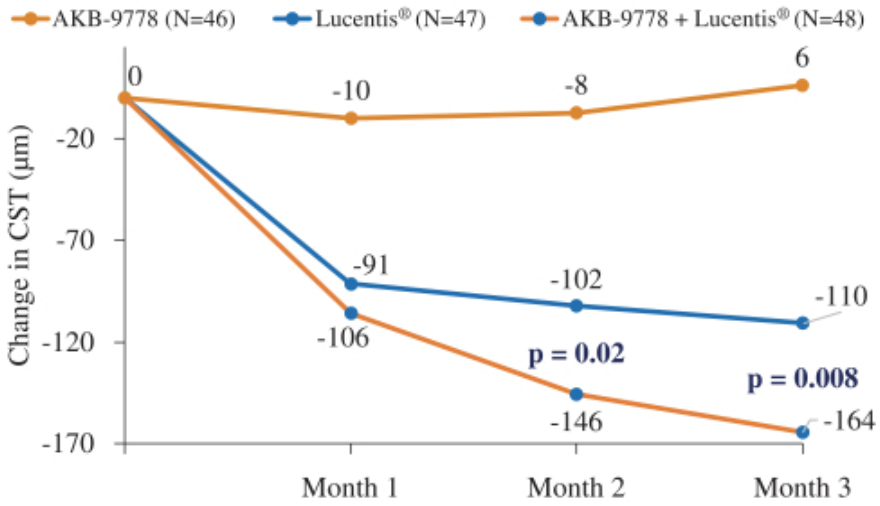

Figure 8. Aggregate Data for Reduction in CST in Phase 2a trial in patients with DME.

Clinical Results in DR

The DR efficacy in the study eyes was assessed in 118 patients with study eyes having DRSS scores of less than seven, which represents mild to severe disease severity, a level of disease that we believe may be reversible.

Because AKB-9778 was dosed systemically we were also able to assess the potential efficacy of AKB-9778 in both the study eye and fellow eyes with underlying DR. Of the 144 patients in this trial, 94 of them had DR in fellow eye, with a DRSS score of less than seven and had not received other treatments during the study treatment period. The severity of DR was assessed using the ETDRS grading of standard retinal photographs. Grading is based on an 11-point scale whose progression is measured through a series of discrete steps. These steps are referred to as the DRSS.

Improvement in diabetic retinopathy severity in study eyes was similar across groups at three months with approximately 10% of patients in each group achieving a two or more-step improvement in DRSS. Importantly, in the study eye, AKB-9778 was associated with approximately the same response rate as Lucentis, which was approved for the treatment of DR. A key difference between these two agents is that Lucentis was administered by an injection into the eye by a clinician while AKB-9778 was administered by subcutaneous injection by the patient, which we believe may result in greater patient compliance due to ease of administration.

The activity of AKB-9778 in the fellow eye was assessed using the same criteria. None of the fellow eyes received any intravitreal injections of Lucentis or sham. Out of the 94 patients with fellow eyes with previously untreated DR, 24 of them received subcutaneous placebo and 70 of them received subcutaneous AKB-9778. In the placebo group, 4.2% of fellow eyes showed 2 or more-step improvement in diabetic retinopathy severity score after three months of treatment, compared to 11.4% of fellow eyes in the AKB-9778 group. The systemic nature of this treatment approach allows AKB-9778 to reach the vasculature of both eyes, potentially treating both eyes with one treatment.

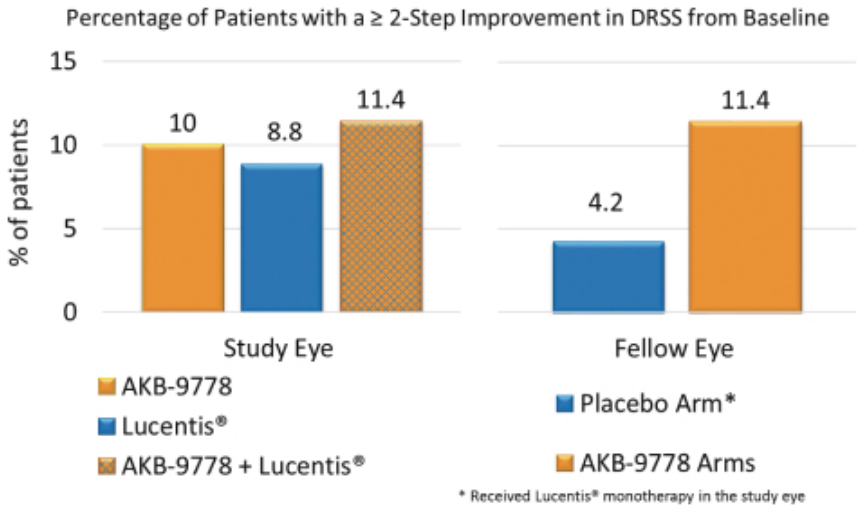

Figure 9. Percent of patients with a 2 or more-step improvement in diabetic retinopathy from baseline to three months in the Phase 2a, TIME-2 trial.

Because the likelihood of development of macular edema or proliferative diabetic retinopathy increases as DR severity increases, which is supported by other contemporaneous studies of diabetic eye disease, we believe improvement of underlying DR or prevention of its progression could reduce visual disability associated with diabetes.

Safety

There was a total of fifteen severe adverse events in the three-month treatment period of the Phase 2a trial with four considered to be treatment-related. Three of these treatment-related events occurred in a single patient who

was enrolled in the Lucentis monotherapy arm and who experienced two severe headaches and one migraine event. A second patient in the AKB-9778 combination therapy group reported a severe treatment-related hypoglycemia event.

Ongoing Phase 2b Clinical Trial in Diabetic Retinopathy

In June 2017, we initiated a Phase 2b clinical trial called TIME-2b. TIME-2b is a double-masked, placebo-controlled multi-center trial that has enrolled 167 patients randomized evenly to receive either AKB-9778 15 mg subcutaneously once daily, AKB-9778 15 mg twice daily or placebo for 48-weeks. The primary endpoint of the TIME-2b study is the percentage of patients who improve by at least 2 steps in DRSS in the study eye. We expect to report topline data from this trial in the second quarter of 2019.

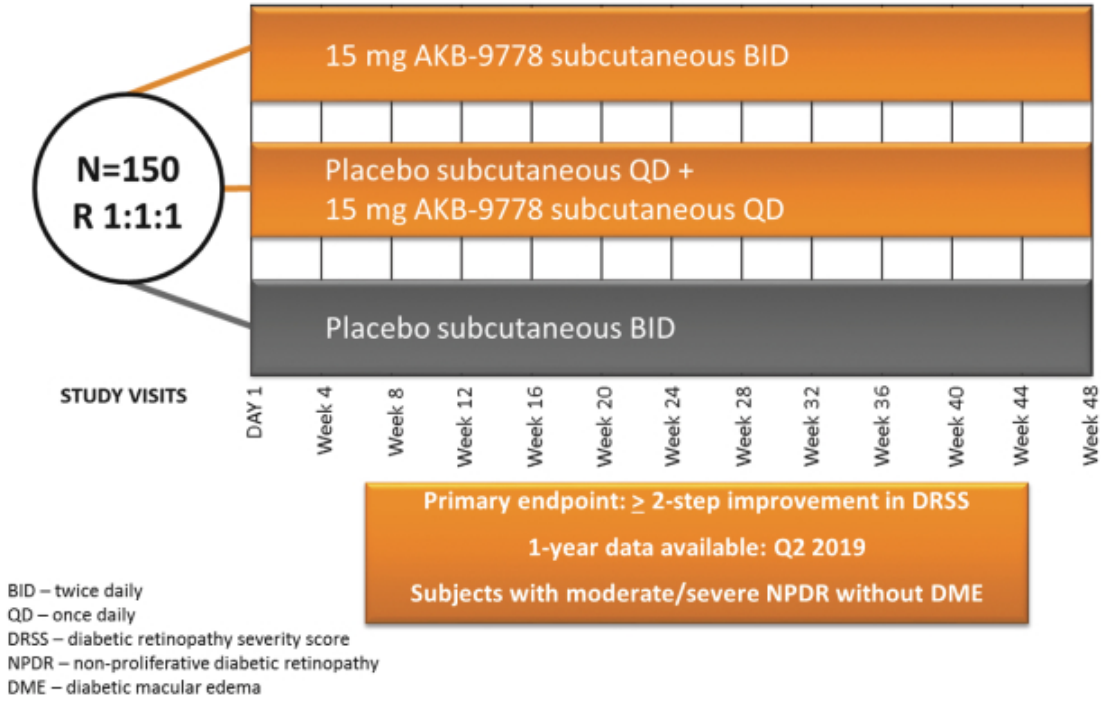

Figure 10. Trial design for Phase 2b trial in DR with AKB-9778

Rationale for Selecting Diabetic Retinopathy as Development Indication

We have chosen to focus our development of AKB-9778 in DR for several reasons:

- Preliminary evidence of efficacy in Phase 2a setting that is similar to FDA-approved treatment (Lucentis)
- Consistent bilateral improvement in study and fellow eye
- Lack of improvement in placebo-treated eyes without active therapeutic is consistent with results from control arm of contemporaneous diabetic retinopathy studies
- Established regulatory path for the treatment of diabetic retinopathy: proportion of patients achieving a two or more-step improvement in diabetic retinopathy severity score compared to placebo at one year

- Patient compliance and convenience benefit of subcutaneous method of administration: reduction of visit and treatment burden
- Potential ability to benefit disease in both eyes
- Potential ability to benefit other vascular beds and
- Opportunity to treat diabetic eye disease at an earlier stage
- High unmet medical need and market potential

Treating patients earlier in the disease process, before the onset of vision-threatening pathology, represents a market opportunity with significant unmet need. Currently, no disease modifying therapy exists for earlier stage DR with the same convenience of AKB-9778. We believe systemic treatment with AKB-9778 has the potential to reverse or prevent vascular damage that is the hallmark of early diabetic eye disease potentially resulting in the delay or prevention of development of advanced complications such as DME and PDR. Lucentis, the only approved therapy for DR, is administered by repeat injections into the eye, and patients with bilateral disease require separate injections in each eye. Furthermore, treatment with Lucentis requires monthly visits to the ophthalmologist. Our internal market research indicates intraocular injections for DR are not favored by patients with early stage disease which is typically bilateral and minimally symptomatic.

We believe AKB-9778 monotherapy provides a promising opportunity for the treatment of early stage DR. As a patient self-administered therapy, AKB-9778 could potentially reduce the burden of treatment and office visits associated with other treatments for diabetic eye disease. This is of importance given emerging evidence that even patients with more advanced disease whose vision is at risk from diabetic eye disease do not visit ophthalmologists and receive treatment on a regular basis. A treatment that does not require an office visit could potentially be a solution to this problem. A majority of patients with early DR will have bilateral disease with fairly well preserved visual acuity. We believe these patients are more likely to accept a therapy based on subcutaneous injections, a delivery method that is already familiar to most diabetics, than an injection into the eye. The systemic nature of this treatment approach allows AKB-9778 to reach the vasculature of both eyes, treating bilateral disease.

If approved by the FDA, AKB-9778 will, to our knowledge, be the only patient self-administered drug to treat non-proliferative diabetic retinopathy with subcutaneous injections, a delivery method that, according to market research we have conducted, is preferred by patients compared to injections into the eye. In addition, AKB-9778 has the potential to decrease the need for the anti-VEGF drugs if it delays or prevents disease progression to DME and/or PDR, an effect we intend to investigate in post marketing studies.

Prevalence studies estimate that roughly one in every three diabetics has underlying diabetic retinopathy while one in every fifteen diabetics has underlying diabetic macular edema. This translates into the DR market being roughly five times larger than the DME market.

The recent approval of Lucentis for all forms of diabetic retinopathy and aflibercept for the treatment of DR in the setting of DME as well as the agreed upon special protocol assessment between Regeneron and the FDA on the Phase III PANORAMA study has established a regulatory path in DR. Our ongoing Phase 2b clinical trial of AKB-9778 is powered to show a statistically significant difference between AKB-9778 and placebo in the proportion of patients improving by 2 or more-steps on the ETDRS diabetic retinopathy severity scale.

Other Potential Systemic Indications

Systemic therapy with AKB-9778 could also provide therapeutic benefits in other areas of the body affected by diabetes, including in the kidneys and the lower extremities. Treatment that could affect vascular compromise in these tissues could potentially prevent or delay the need for more extreme interventions such as kidney dialysis or amputation. We have included exploratory endpoints in our on-going Phase 2b trial of AKB-9778 in early-

stage DR to study the effects of AKB-9778 on parameters of diabetic kidney disease, including but not limited to urine albumin creatinine ratio. If approved for such indications, we believe that systemic treatment with AKB-9778 has the potential to change the treatment paradigm for diabetics and solve a major societal problem by lowering the cost of care associated with diabetic complications. This societal cost is significant as diabetic complications are estimated to cost the health care system 3.5 times more than patients without complications. For example, dialysis patients cost an average of $89,000 per year and the cost for the first year of DME therapy with Eylea® is $14,400 per eye based on published Medicare allowable charges per dose and the frequency of dosing as approved by the FDA.

AKB-9778 in Primary Open Angle Glaucoma

Unmet medical need:

POAG is a leading cause of blindness affecting approximately 64.3 million people worldwide in 2013 with an expected increase to 76.0 million in 2020 and 118.0 million by 2040. POAG is characterized by optic nerve and neuroretina anomalies and progressive visual field defects. Elevated intraocular pressure, or IOP, is the primary modifiable risk factor and reducing IOP is the only clinical approach shown to slow or prevent vision loss. Despite the availability of effective IOP lowering drugs, many patients require multiple agents to control IOP that together often fail to achieve target IOP. The conventional outflow pathway, consisting of the trabecular meshwork and a specialized vessel called Schlemm's canal, controls IOP and has been identified as the site of increased resistance to aqueous humor outflow in POAG. Importantly, most current POAG therapies do not target conventional outflow, and reduce IOP by either decreasing the formation of aqueous humor or facilitating non-conventional outflow pathways. The failure of most current therapies to modify conventional outflow has been hypothesized to contribute to continued deterioration of conventional outflow and progressive increases in IOP over time. We believe that developing agents that target conventional outflow pathology directly will likely have improved therapeutic potential alone or in combination with approved glaucoma agents and may prevent progression of POAG that often occurs despite current therapy.

Emerging role of the Tie2 Pathway in the maintenance of conventional outflow:

Recently, two independent groups have shown that Tie2 is expressed and activated in Schlemm's canal endothelial cells during development and in the mature vessel. Disruption of the Tie2 pathway in mice by conditional knockout early in postnatal development results in failure of the formation of Schlemm's canal, associated with increased IOP and with retinal and optic nerve pathology resembling human congenital glaucoma. Tie2 pathway disruption later in postnatal development results in degeneration of Schlemm's canal with development of increased IOP and retinal and optic pathology reminiscent of POAG[23]. Tie2 is most highly expressed in mature Schlemm's canal inner wall endothelium and disruption of the Tie2 pathway results in increased cell death, or apoptosis, and reduced formation of giant vacuoles consistent with compromised conventional outflow. Supporting these preclinical findings, Tie2 loss of function variants were identified in 10 of 189 unrelated primary congenital glaucoma families, and SNPs in the Ang-1 promoter region were significantly associated with the risk of POAG[25-28]. We believe that these preclinical findings along with human genetic evidence provides a sound scientific premise that activation of the Tie2 pathway in Schlemm's canal could provide a novel conventional outflow-targeted POAG therapy.

Role of VE-PTP in Signaling Pathways and Relevance to Glaucoma

Aerpio has developed first-in-class, potent and selective small molecule inhibitors of the catalytic domain of VE-PTP. In vascular endothelial cells, AKB-9778, Aerpio's lead VE-PTP inhibitor, activates Tie2 and triggers signaling pathways downstream of Tie2 that have been implicated in modulation of conventional outflow

facility. These include endothelial nitric oxide synthase, or eNOS, activation and Rho pathway inhibition via Rac1.

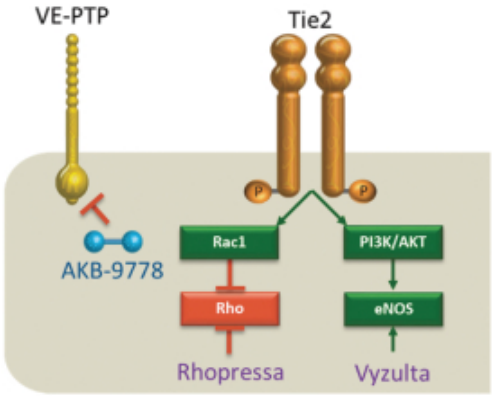

Figure 11. VE-PTP inhibition as a novel conventional outflow targeted approach for glaucoma treatment. Activation of Tie2, with AKB-9778, affects pathways commonly associated with reduction of intraocular pressure. Rhopressa and Vyzulta are recently approved glaucoma drugs which block the Rho pathway and stimulate the eNOS pathway, respectively. Inhibition of VE-PTP should provide both benefits, blocking Rho and stimulating eNOS.

Evidence Supporting Tie2 Activation as a Conventional Outflow Glaucoma Target:

In a completed Phase 2a clinical trial, patients receiving subcutaneous AKB-9778 demonstrated a statistically significant reduction from baseline in IOP compared to those receiving subcutaneous placebo injections. These IOP reductions were detected in individuals with normal ocular pressure in a study not designed to measure IOP changes and were of the same magnitude as reductions seen in individuals with normal ocular pressure on oral ß-blocker therapy. Moreover, patients with baseline IOP greater than or equal to 16 mmHg had larger reductions in IOP than those with baseline IOP less than 16 mmHg, consistent with effects on pressure dependent conventional outflow.

	AKB-9778 Monotherapy		AKB-9778 + Lucentis®		Lucentis® monotherapy	
	SE	FE	SE	FE	SE	FE
Mean Baseline IOP (mmHG)	15.8	15.4	15.9	16.1	15.2	15.8
Mean Δ from BL (mmHG)	**-1.4**	**-1.4**	**-1.0**	**-1.5**	0.1	-0.1
t-test Δ BL-Mo 3 (p-value)	**<0.01**	**<0.01**	**<0.05**	**<0.01**	0.88	0.84

BL = baseline; SE = study eye; FE = Fellow eye; SD = standard deviation

Figure 12. Subcutaneous administration of AKB-9778 significantly reduces IOP in patients with normal ocular pressure.

Preclinical Data Supporting Topical Ocular Delivery of AKB-9778:

Based on preliminary clinical proof-of-concept by subcutaneous administration of AKB-9778, Aerpio is advancing a topical ocular program for AKB-9778 as a conventional outflow-targeted approach to the treatment

of patients with POAG or ocular hypertension. AKB-9778 is soluble in aqueous solution and preliminary topical ocular studies in rabbits have demonstrated good tolerability, superior aqueous humor exposure and IOP lowering compared to subcutaneous administration. The AKB-9778 topical formulation was well tolerated and exposure was demonstrated in the aqueous humor following two days of three times a day 30 µL topical ocular administration to both eyes of Dutch Belted rabbits. These data suggest that a topical ocular formulation of AKB-9778 may be sufficient to deliver AKB-9778 to target ocular tissues with acceptable tolerability.

The AKB-9778 topical ocular formulation was also well tolerated following seven days of once daily, or QD, and twice daily, or BID, 30 µL topical ocular administration to both eyes in New Zealand White Rabbits with normal ocular pressure, and demonstrated a dose-dependent and statistically significant reduction in IOP of both QD and BID topical ocular dosing at the highest dose level, as shown in the figure below. Reduction in IOP persisted for at least 24 hours following the last dosing period.

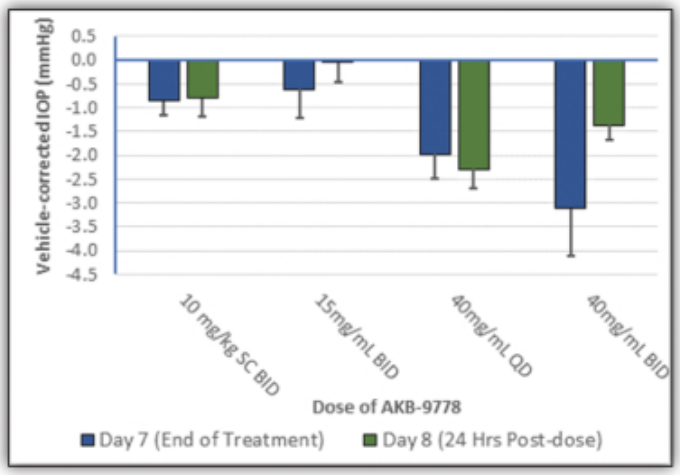

Figure 13. IOP effects of topical ocular compared to subcutaneous AKB-9778 in male rabbits. High dose topical ocular (40 mg/ml) AKB-9778 administered either QD or BID reduced IOP more than low dose topical (15 mg/ml) or subcutaneous (10 mg/kg) administration BID (Day 7). IOP effects persisted 24 hours post dose (Day 8).

We plan to initiate a Phase 1b study to evaluate the potential of topical AKB-9778 to lower IOP in the first half of 2019, with top-line results expected to be available by the third quarter of 2019.

AKB-4924 for Inflammatory Bowel Disease

AKB-4924 works by inhibiting HIF prolyl-hydroxylase enzymes. Unlike other compounds currently in development that act broadly against all forms of HIF, AKB-4924 selectively stabilizes a specific form of HIF, HIF-1 alpha. HIF-1 alpha has a profound effect on innate immunity and epithelial barrier function. However, HIF-1alpha differs from HIF-2, in that it does not stimulate the formation of new red blood cells. That characteristic of greater selectivity could, we believe, make AKB-4924 a more attractive means to target HIF in IBD. We have tested AKB-4924 in multiple preclinical models of IBD and it has shown promising activity in these models. We recently completed a Phase 1a single-ascending dose trial in healthy volunteers with orally administered AKB-4924. We observed a consistent dose/exposure relationship with no notable adverse events at any dose level. Importantly, we observed no stimulation of erythropoietin expression, an effect which could lead to a dose-limiting safety effect. Based on preclinical data, we believe that AKB-4924 has therapeutic potential for

the treatment of IBD via a once-daily, oral route of administration. We believe that the potency, selectivity, activity in animal models, and the ability to dose AKB-4924 orally distinguish it from other agents targeting this pathway.

We plan on developing AKB-4924 as a once-daily oral pill for the treatment of inflammatory bowel disease, or IBD. IBD is a group of inflammatory and autoimmune conditions that affect the gastrointestinal tract, typically resulting in severe abdominal pain, weight loss, vomiting and diarrhea. The most common forms of IBD include ulcerative colitis and Crohn's disease, which are estimated to affect approximately 3 million people in the United States. Chronic IBD can be a debilitating condition, and advanced cases may require surgery to remove the affected region of the bowel. Based on the data observed in preclinical and clinical studies to date, we believe that AKB-4924 may have advantages over other products that are either currently approved or in late stage development for IBD.

Current therapies are primarily focused on broad spectrum immunosuppressants which only indirectly promote healing of damaged tissue. In contrast, HIF-1 alpha stabilization has been shown to selectively reduce inflammation as well as directly stimulate restoration of the intestinal barrier in animal models and thus we believe represents an attractive novel target.

Current IBD Treatments

Current therapies are primarily focused on broad spectrum anti-inflammatory molecules or immunosuppressants which only indirectly promote healing of damaged tissue. These therapies include aminosalicylate derivatives such as mesalazine, corticosteroids such as prednisone, and immunomodulatory biologics such as infliximab. Each of these therapies is associated with their own side effects ranging from hypersensitivity to increasing the risks of developing malignancies or reactivation of latent viral infections.

While reducing inflammation and modulating the immune response address key pathological processes in IBD, these approaches do not directly target some of the underlying causes of the disease. Those causes include defects in the cell-to-cell junctions of the intestinal cell wall that can lead to the triggering of the immune system. HIF-1 alpha stabilization has been shown to selectively reduce inflammation as well as directly stimulate restoration of this intestinal barrier in animal models, and, thus, represents an attractive novel approach to treating this disease.

Our Solution AKB-4924

We believe that, if approved, AKB-4924 provides a solution to all the major unmet needs in IBD. We have tested AKB-4924 in multiple models including chemical and immune-mediated disease. We have observed consistent and promising activity across these models. Based on our pre-clinical toxicology program to date, we have observed no signs of secondary malignancies, immunosuppression, risk of opportunistic infection or immunogenicity, adverse events that have all been seen in clinical studies of agents that are currently approved for treatment of or being studied in the treatment of IBD. We plan to develop AKB-4924 as a once a day, oral tablet, which we believe is a preferred route of administration compared to the biologics commonly used as first

line therapy, which require parenteral administration. Taken together, we believe that AKB-4924, if approved, has the potential to be the preferred first-line treatment for patients with moderate-severe inflammatory bowel disease.

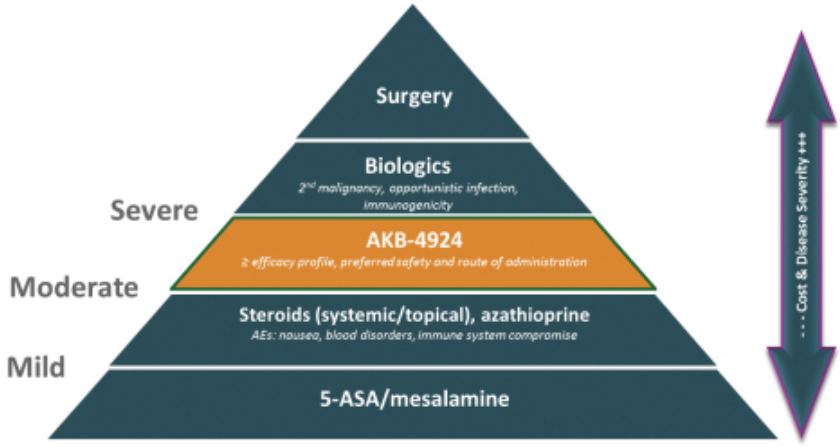

Figure 14. Potential for AKB-4924 in the treatment of inflammatory bowel disease

Preclinical Data for AKB-4924

In preclinical models of inflammatory bowel disease, AKB-4924 significantly improved disease in both the maintenance and induction treatment modes, including reducing key inflammatory cytokines and increasing the expression of mucosal wound healing factors. In a mouse model of colitis 2,4,6-trinitrobenzenesulfonic acid, or TNBS, is used to induce severe inflammation in the colon resulting in multiple symptoms that mimic human disease including easy to measure signs such as weight loss. Oral dosing of 5 mg/kg AKB-4924 showed significant levels of recovery from this weight loss within four days. In addition, levels of inflammatory

cytokines including interleukin 1 beta, TNFalpha, interleukin 12 p70, and interleukin 6 were significantly reduced in animals receiving AKB-4924 ($p < 0.05$ in all cases).

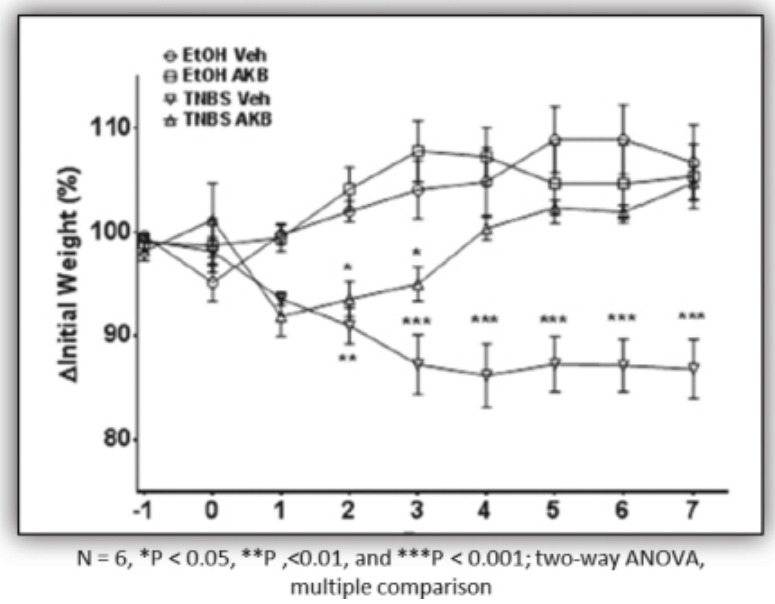

Figure 15. Orally dosed AKB-4924 (5 mg/kg) reverses weight loss induced by trinitrobezenesulfonic acid (TNBS) colitis.

AKB-4924 was also tested in an alternate model of IBD induced by overexpression of tumor necrosis factor-alpha (TNF-alpha) in a model of Crohn's Disease known as the DARE model. In this model, the induced high levels of TNF-alpha lead to the development of Crohn's-like disease due to inflammation of intestinal tissues or

ileitis. AKB-4924 administered at 5 mg/kg improved ileitis and led to significantly reduced overall inflammation in the intestine.

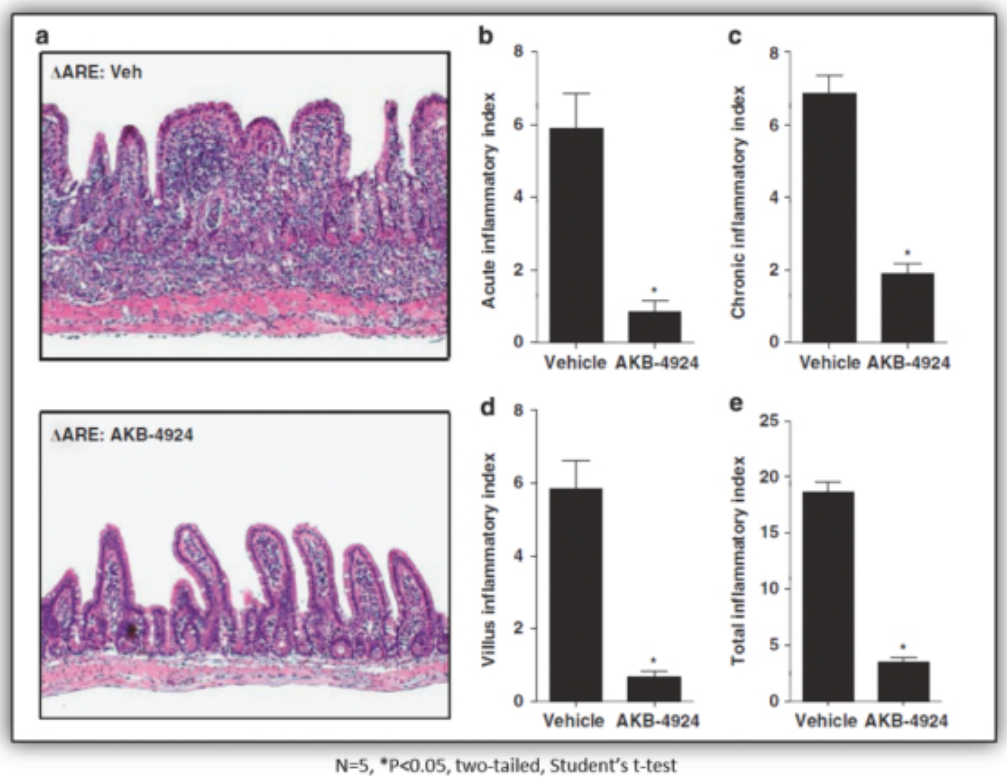

Figure 16. Terminal ileitis in control animals (a-top panel), terminal ileitis was completely reversed via administration of AKB-4924 (a-bottom panel). AKB-4924 administration resulted in a decrease of all inflammatory scores.

Clinical Data for AKB-4924

To date, AKB-4924 has completed a single-ascending dose trial in healthy male volunteers. Healthy volunteers were given a single oral dose of AKB-4924 of 20mg, 60mg, 120 mg, or 240 mg. Findings from this trial support the safety, local activity, selective HIF-1alpha stabilization, and dose dependent exposure of oral AKB-4924. Consistent with the selectivity of AKB-4924 for HIF-1alpha, there were no significant changes in levels of circulating erythropoietin (EPO) in this trial. Other studies have shown that regulation of EPO is primarily dependent on the activity of HIF-2.

We believe that the data observed in nonclinical and clinical studies with orally administered AKB-4924 provide a compelling rationale to advance its development for the treatment of inflammatory bowel disease.

ARP-1536

ARP-1536 is a humanized monoclonal antibody currently in preclinical development that is directed at the same target as AKB-9778. ARP-1536 binds the extracellular domain of VE-PTP inhibiting its ability to interact with

Tie2. Our preclinical development program has shown that inhibiting VE-PTP with an antibody results in an activity profile similar to AKB-9778 in a number of different models of retinopathy. We are evaluating development options for ARP-1536, including once-monthly subcutaneous injection for the treatment of diabetic vascular complications and once-monthly intravitreal injection for advanced diabetic eye disease, such as DME and PDR.

Intellectual Property

As of September 30, 2017, we owned at least 31 U.S. patents, at least 18 pending U.S. provisional or non-provisional patent applications, at least 268 foreign patents, and at least 143 pending foreign applications, and a had a non-exclusive license to one U.S. patent, with claims directed toward various aspects of our product candidates and research programs. Specifically, the claims of these patents and patent applications include compositions of matter, methods of use, drug product formulations, and methods of manufacture. Such patents and patent applications, if issued, are expected to expire on various dates from 2027 to 2037, without taking into account any possible patent term adjustments or extensions. Within the foregoing patent portfolio, as of September 30, 2017, we owned at least 3 U.S. patents, at least 6 pending U.S. provisional or non-provisional patent applications, at least 17 foreign patents, and at least 27 pending foreign applications that are directed toward ARP-1536, and formulations or uses thereof. As of September 30, 2017, within the foregoing patent portfolio, we owned at least 19 U.S. patents, at least 12 pending U.S. provisional or non-provisional patent applications, at least 161 foreign patents, and at least 85 pending foreign applications that are directed toward AKB-9778, and formulations, medicinal chemistry variants, or uses thereof. As of September 30, 2017, within the foregoing patent portfolio, we owned at least 9 U.S. patents, at least 1 pending U.S. provisional or non-provisional patent application, at least 90 foreign patents, and at least 31 pending foreign applications, and had 1 non-exclusively in-licensed U.S. patent that are directed toward AKB-4924, and formulations, manufacturing processes, medicinal chemistry variants, or uses thereof. Such patents claiming compositions of matter directed toward ARP-1536 are set to expire in 2027, without taking into account any possible patent term adjustments or extensions. Such patents claiming compositions of matter directed toward AKB-9778 are set to expire in 2027, without taking into account any possible patent term adjustments or extensions. Such patents claiming compositions of matter directed toward AKB-4924 are set to expire in 2030, without taking into account any possible patent term adjustments or extensions.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technologies, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

There are a number of currently marketed products and product candidates in preclinical research and clinical development by third parties to treat the various diseases that we are targeting. If AKB-9778 and our other product candidates are approved for the indications that we are targeting, they will compete with the products and product candidates discussed below.

DR—Lucentis was recently approved to treat patients with DR. In addition, laser photocoagulation is sometimes used to treat DR prior to the onset of DME and temporarily prevent further vision loss. The anti-VEGF agent, Eylea (aflibercept), which is injected into the eye, is in a Phase 3 study for DR without DME, entitled PANORAMA. In addition, we are aware that there are a number of other companies that are actively developing product candidates for the treatment of DR without DME.

DME—The principal competitors for our program in DME are the anti-Ang-2 antibodies REGN-910 (nesvacumab) and RG7716 (bi-specific antibody which targets VEGF-A and Ang-2). Both of these compounds are in Phase 2 studies in DME, RUBY and BOULEVARD, respectively.

IBD—Current therapies for IBD include anti-inflammatory molecules, or immunosuppressants such as aminosalicylate derivatives, corticosteroids, and immunomodulatory biologics. In addition, we are aware that there are a number of other companies that are actively developing product candidates for the treatment of IBD, including: filgotinib; ozanimod; mongresen; ABT-494; ADP-334; MT-1303; PTG-100; TD-1473; amongst others.

Sales and Marketing

We hold worldwide commercialization rights to all of our product candidates. Subject to receiving marketing approval, we intend to independently pursue the commercialization of AKB-9778 in the United States for DR by building a focused sales and marketing organization in these geographies. We believe that such an organization will be able to address the community of physicians who are key specialists in treating the patient populations for which our product candidates are being developed.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Outside of the United States, we intend to pursue the approval and commercialization of AKB-9778 for DR through strategic collaborations. We may develop and commercialize AKB-9778 for other indications either independently or through collaborations with third parties. We may develop and commercialize AKB-4924, subject to receiving additional funding, which we may seek to obtain in connection with a collaboration with a strategic and commercial partner. We may also develop and commercialize ARP-1536, subject to receiving additional funding, which may be from a collaboration with a strategic or commercial partner.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We have relied on and intend to continue to rely on qualified third-party contract manufacturers to produce our product candidates, including clinical supplies to support our clinical trials. We expect that commercial quantities of any compound and materials for our product candidates, if approved, will be manufactured in facilities and by processes that comply with FDA and other regulations. At the appropriate time in the product development process, we will determine whether to establish manufacturing facilities or continue to rely on third parties to manufacture commercial quantities of any products that we may successfully develop.

Government Regulation

Government authorities in the United States, including federal, state, and local authorities, and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of pharmaceutical and biological products, such as those we are developing. In addition, some government authorities regulate the pricing of such products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA and the Public Health Service Act, or PHSA, and its implementing regulations. FDA approval is required before any new unapproved drug or biologic or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Drugs and biologics are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of extensive nonclinical laboratory tests and nonclinical animal studies, all performed in accordance with the Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin and must be updated annually;
- approval by an independent institutional review board, or IRB, or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of a biologics license application, or BLA, or a new drug application, or NDA, after completion of all pivotal clinical trials;
- review of the product application by an FDA advisory committee, where appropriate and if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the proposed product is produced to assess compliance with current Good Manufacturing Practices, or cGMP;
- satisfactory completion of any FDA audits of the clinical study sites to assure compliance with GCPs, and the integrity of clinical data in support of the BLA or NDA; and
- FDA review and approval of a BLA for a biologic drug candidate that is safe, pure, and potent or an NDA for a drug candidate that is safe and effective prior to any commercial marketing or sale of the product in the United States.

The nonclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

An IND is a request for authorization from the FDA to administer an investigational new drug or biological product to humans in clinical trials. The central focus of an IND submission is on the general investigational plan, the protocol(s) for human trials, and the safety of study participants. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or

questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. The FDA may impose a clinical hold at any time during clinical trials and may impose a partial clinical hold that would limit trials, for example, to certain doses or for a certain length of time.

Clinical Trials

Clinical trials involve the administration of the investigational new drug or biological product to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practices, or GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical trial site's institutional review board, or IRB, before the trials may be initiated, and the IRB must monitor the trial until completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

The clinical investigation of a drug or biological product is generally divided into three or four phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

- *Phase 1.* The drug or biological product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- *Phase 2.* The investigational product is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.
- *Phase 3.* The investigational product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety (or safety, purity, and potency for biological products), to evaluate the overall benefit-risk profile of the investigational product, and to provide an adequate basis for physician labeling.
- *Phase 4.* In some cases, the FDA may condition approval of a BLA or NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after approval. In other cases, a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the drug or biological product. Such post-approval studies are typically referred to as Phase 4 clinical trials.

Sponsors must also report to the FDA, within certain timeframes, serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product candidate. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives or competitive climate.

Submission of a BLA or NDA to the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of a BLA or NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most BLAs and NDAs is subject to an application user fee. For fiscal year 2018, the application user fee is $2,421,495, and the sponsor of an approved BLA or NDA is also subject to an annual program fee of $304,162 for each approved prescription drug or biological product on the market. These fees are typically increased annually. Applications for orphan drug products are exempted from the BLA and NDA user fees and may be exempted from program fees, unless the application includes an indication for other than a rare disease or condition.

A BLA or NDA must include all relevant data available from pertinent nonclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including trials initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an application for filing. Once a BLA or NDA has been accepted for filing, the FDA's goal for novel drug and biological products generally is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by the FDA's requests for additional information or clarification.

Before approving a BLA or NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA or NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA is required to refer an application for a novel drug or biological product to an advisory committee or explain why such referral was not made. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on a BLA or NDA

After the FDA evaluates the BLA or NDA and conducts relevant inspections, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter will identify the deficiencies that prevent the FDA from approving the application and may require additional clinical data or an additional Phase 3 clinical trial(s), or other significant, expensive and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the BLA or NDA does not satisfy the criteria for approval and issue a denial.

The FDA could also approve the BLA or NDA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure

safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

New government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of BLAs and NDAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs. The key benefits of fast track designation are more frequent interactions with the FDA during development and testing, the eligibility for priority review, and rolling review, which is submission of portions of an application before the complete marketing application is submitted.

Based on results of the Phase 3 clinical trial(s) submitted in a BLA or NDA, the FDA may grant the BLA or NDA a priority review designation, which sets the target date for FDA action on the application for a novel product at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve a BLA or NDA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing trials or completion of ongoing trials after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit.

In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated, and,

depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates, and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved BLA or NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, untitled or warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending BLAs or NDAs or supplements to approved BLAs or NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Pediatric Trials and Exclusivity

A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within sixty days of an end of Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. Development program candidates designated as orphan drugs are exempt from the above requirements. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA or NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-requested pediatric trials are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection covering the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application relying on the BLA or NDA sponsor's data.

Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA or NDA, plus the time between the submission date and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of the product's approval. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA or NDA.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the proposed biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the nonclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is the same as the RLD with respect to the active ingredient(s), the route of administration, the dosage form, the strength of the drug and the labeling (with certain exceptions). At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if "the rate and extent of absorption of the [generic] drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . ."

Upon approval of an ANDA, the FDA assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider an "A" therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of an "A" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA (or a 505(b)(2) NDA, which is a marketing application in which sponsors may rely on investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted) may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, discussed below, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA or 505(b)(2) applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA or 505(b)(2) applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge a listed patent, the ANDA or 505(b)(2) application will not be approved until the listed patent expires (unless the patent claims only a method-of-using the referenced product and the ANDA or 505(b)(2) applicant indicates that it is not seeking approval of the claimed method of use).

If the applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been

accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of expiration of the patent, a decision in the infringement case that is favorable to the ANDA or 505(b)(2) applicant, or 30 months after the receipt of the Paragraph IV notice (which can be extended if the reference product has 5-year exclusivity and the ANDA or 505(b)(2) application is submitted between 4 and 5 years after approval of the reference product).

European Union/Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union and in other jurisdictions, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial authorization application, or CTA, must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical trial may proceed.

The requirements and process governing the conduct of clinical trials vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under European Union regulatory systems, we must submit a marketing authorization application. The content of the BLA or NDA filed in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.
Countries that are part of the European Union, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical and biologic products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Authorization Procedures in the European Union

Medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

- *Centralized procedure.* The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area,

or EEA, which is comprised of the 28 member states of the European Union plus Norway, Iceland, and Lichtenstein. This procedure results in a single marketing authorization issued by the EMA that is valid across the EEA. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.

- For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Commission following a favorable opinion by the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.
- *National authorization procedures.* There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:
- *Decentralized procedure.* Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In some cases, a Pediatric Investigation Plan, or PIP, or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application. A PIP describes, among other things, proposed pediatric trials and their timing relative to clinical trials in adults.

New Chemical Entity Exclusivity

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Accelerated Review

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA's Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third- party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Some of the provisions of the Affordable Care Act have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. Thus, the full impact of the Affordable Care Act, or any law replacing elements of it, on our business remains unclear. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result,

increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal Physician Payment Sunshine Act, that requires drug and biologics manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Affordable Care Act broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

We are also subject to the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business and requires companies to maintain accurate books and records and a system of internal accounting controls. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, including environmental, health and safety laws and regulations, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Employees

As of September 30, 2017, we had 23 full-time or part-time employees, including 12 employees with doctorate level degrees. Of these employees, 17 employees are engaged in research and development activities and 6 employees are engaged in general and administrative activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider the relationship with our employees to be good.

Facilities

We occupy approximately 7,580 rentable square feet of office and laboratory space in Ohio under a lease that expires on June 30, 2018. We have an option to extend the lease term until June 30, 2021. We believe that this office and laboratory space is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Legal Proceedings

We are not currently subject to any material legal proceedings.

MANAGEMENT

The following table sets forth certain information concerning our executive officers and directors as of December 31, 2017:

Name	Age	Position(s)
Executive Officers		
Stephen Hoffman	63	Chief Executive Officer and Director
Joseph Gardner	62	President, Founder and Director
Michael Rogers	58	Chief Financial Officer
Steve Pakola	49	Chief Medical Officer
Kevin G. Peters	61	Chief Scientific Officer
Non-Employee Directors		
Muneer Satter(3)	57	Director, Chairman
Paul M. Weiss(2)	59	Director
Caley Castelein(1)	47	Director
Anupam Dalal(2)	46	Director
Steven Prelack(1)	60	Director
Chau Khuong(3)	41	Director
Pravin Dugel(1)	54	Director

(1) Member of audit committee.
(2) Member of compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Stephen Hoffman, M.D., Ph.D. has served as Aerpio's Chief Executive Officer since December 2017. From February 2014 until joining Aerpio, Dr. Hoffman was a Senior Advisor at PDL BioPharma, an investment firm that manages a portfolio of investments in companies, products, royalty agreements and debt facilities in the biotech, pharmaceutical and medical device industries. Prior to that he served as a Managing Director at Skyline Ventures, a venture capital firm, from 2007 to 2014 and was general partner at TVM Capital from 2003 to 2007. Prior to TVM, he served as President, Chief Executive Officer and a Director of Allos Therapeutics from 1994 to 2002, where he remained as Chairman until its acquisition by Spectrum Pharmaceuticals, Inc. in 2012. Dr. Hoffman currently serves on the board of directors of Dicerna Pharmaceuticals, Inc., AcelRx Pharmaceuticals, Inc., Bicycle Therapeutics Ltd., and Palleon Pharmaceuticals, Inc. Dr. Hoffman completed a fellowship in clinical oncology and a residency and fellowship in dermatology from 1990 to 1994, both at the University of Colorado, and holds a Ph.D. in chemistry from Northwestern University and an M.D. from the University of Colorado School of Medicine. He is also board-certified in Dermatology. We believe that Dr. Hoffman is qualified to serve as our Chief Executive Officer and on our board of directors based on his industry experience and service on multiple boards.

Joseph Gardner, Ph.D. has served as Aerpio's President and Founder since December 2011 and served as its Chief Executive Officer from December 2011 until December 2017. Dr. Gardner co-founded Akebia Therapeutics in 2007 and has been an Advisor for Akebia since 2013. He served as the Chief Executive Officer, President and as a member of the board of directors of Akebia until September 2013. Prior to that, Dr. Gardner worked in pharmaceutical discovery and development at Procter & Gamble Pharmaceuticals for 23 years, including two years in P&G's health care mergers and acquisition group and 10 years managing discovery licensing. He served as a Director of Chemistry and Intellectual Property Management of the Pharmaceutical Division of Procter & Gamble, and as a Director of Juvenile Diabetes Research Foundation International Inc. Dr. Gardner received his B.S. with honors in Biological Chemistry from Tulane University in 1977, earned his M.S. in Chemistry in 1980 from Utah State University and Ph.D. in 1983 in Medicinal Chemistry from

University of Wisconsin. We believe that based on Dr. Gardner's knowledge of our company, industry and business and his service as our former Chief Executive Officer and President, Dr. Gardner is qualified to serve on our board of directors.

Michael Rogers has served as Aerpio's Chief Financial Officer since November 2017. From 2016 to 2017, Mr. Rogers served as a consultant to healthcare companies. Prior to that, Mr. Rogers was the chief financial officer at Acorda Therapeutics, a biopharmaceutical company, from 2013 to 2016. Prior to Acorda Therapeutics, he was the Executive Vice President and chief financial officer of BG Medicine from 2009 to 2012. From 1999 to 2009, Mr. Rogers was the chief financial officer of Indevus Pharmaceuticals until the company's sale to Endo Pharmaceuticals. He also served as chief financial officer at Advanced Health Corporation and Autoimmune. Prior to his roles as chief financial officer, Mr. Rogers was an investment banker at Lehman Brothers and PaineWebber, where he focused on life sciences companies. Mr. Rogers received his B.A. from Union College, and an M.B.A. from the Darden School of Business at the University of Virginia. He currently serves as Chairman of the Board of Directors of Keryx Biopharmaceuticals and as a member of the Board of Directors for pSivida Corp.

Steve Pakola, M.D. has served as Aerpio's Chief Medical Officer since October 2015. Since May 2012, Dr. Pakola has served as the Chief Medical Officer of Amakem NV and the Chief Medical Officer, Senior Vice President of Clinical Development and as Director at ThromboGenics NV from 2000 to 2012. Previously, Dr. Pakola served as an Associate Director of Cardiovascular Clinical Research at Boehringer-Ingelheim Pharmaceuticals, where he served as Global Medical Lead on the Lipid-Lowering Development Programme, as well as USA Medical Lead for the Direct Thrombin Inhibitor Development Programme. From 1996 to 1998, Dr. Pakola served in senior-level clinical development positions at Quintiles Cardiovascular Therapeutics and Organon. Dr. Pakola received his B.A and his MD from the University of Pennsylvania.

Kevin G. Peters, M.D. has served as Aerpio's Chief Scientific Officer since November 2011. Dr. Peters guided the development of AKB-9778 while at Akebia Therapeutics, and continues to be in charge of scientific discovery and development for Aerpio. From 2006 to 2010 he served as Medical Director of Cardiovascular and Metabolic Disease in Global and Discovery Medicine at Bristol Myers Squibb and from 1998 to 2006 he served as head of Therapeutic Angiogenesis research at P&G Pharmaceuticals. He served as a Member of the Scientific Advisory Board of Akebia. Dr. Peters served as an Associate Professor of Medicine and Pharmacology in the Division of Cardiology at Duke University Medical Center. Dr. Peters received his M.D. from the University of Iowa and B.A. from Augustana College.

Board Composition

Non-Employee Directors

Muneer A. Satter has served as a member of Aerpio's board of directors since October 2013. Mr. Satter has been Founder and Managing Partner of Satter Medical Technology Partners, L.P. since 2016, Chairman of Satter Investment Management LLC since 2012, and he also manages the Satter Foundation. Prior to Satter Investment Management, Mr. Satter was a partner at Goldman Sachs where he spent 24 years in various roles, most recently as the Global Head of the Mezzanine Group in the Merchant Banking Division, where he raised and managed over $30 billion of assets. Mr. Satter is chairman of the board of directors of Akebia Therapeutics and Restorsea Holdings, LLC and a director of Vital Therapies, Inc., Linq3 Technologies LLC and Annexon Biosciences. He also serves as vice chairman of Goldman Sachs Foundation and GS Gives, is a director of World Business Chicago, is on the Board of Advisors of the American Enterprise Institute, is on the Board of Directors of the Navy SEAL Foundation, and is on the Board of Trustees of Northwestern University where he is Chairman of the Finance Committee. Mr. Satter received a B.A. in Economics from Northwestern University, a J.D. from Harvard Law School and an M.B.A. from Harvard Business School. We believe that Mr. Satter is qualified to serve on our board of directors due to his extensive investment experience.

Paul M. Weiss Ph.D. has served on Aerpio's board of directors since November 2011. Since 2006, Dr. Weiss has been Managing Director of Venture Investors. From 2001 to 2006 Dr. Weiss served as the President at Gala

Design, which was sold to Cardinal Health (now part of Catalent). From 1997 to 2000, Dr. Weiss served as the VP of Business Development/VP of Technology and Product Licensing at 3-Dimensional Pharmaceuticals (IPO and subsequent sale to Johnson & Johnson). Prior to that, Dr. Weiss worked as Director of Licensing for the pharmaceutical company Wyeth-Ayerst (now part of Pfizer). Currently, he also serves as a director at FluGen and Madison Vaccines. He served as a director of Akebia Therapeutics (Nasdaq: AKBA), Tissue Regeneration Systems, and Neurovance (sold to Otsuka). Dr. Weiss holds a Ph.D. in Biochemistry and an M.B.A. from the University of Wisconsin-Madison and a B.Sc. in Biochemistry from Carleton University Institute of Biochemistry. We believe Dr. Weiss is qualified to serve on our board based on his industry experience and service on multiple boards.

Caley Castelein, M.D. has served on Aerpio's board of directors since March 2017. Dr. Castelein is the Founder and has been a Managing Director for Kearny Venture Partners since 2006. Dr. Castelein is also the Founder and has been the Managing Director for KVP Capital since 2013. He is a director for ViewRay, Alivecor, Boreal and Newbridge Pharmaceuticals. Dr. Castelein received his M.D. from University of California, San Francisco and his A.B. in Biology from Harvard University. We believe that Dr. Castelein is qualified to serve as a director based on his industry experience and service on multiple company boards.

Anupam Dalal, M.D. has served on Aerpio's board of directors since November 2011. Since August 1, 2016, Dr. Dalal has been working at Acuta Capital. From 2006 to 2016, Dr. Dalal was the Managing Director of Kearny Venture Partners. He was a Founder and Managing Member of KVP Capital. He served as a director of Akebia Therapeutics from 2008 to 2016. Dr. Dalal received an M.D. degree from the University of California in San Francisco with honors; an M.B.A., with distinction, from Harvard Business School; and a B.A. degree in Economics, Phi Beta Kappa and highest honors, from the University of California at Berkeley. We believe that Dr. Dalal is qualified to serve as a director based on his industry experience.

Steven Prelack has served on Aerpio's board of directors since March 2017. Mr. Prelack has been the Chief Operating Officer and Senior Vice President of VetCor since 2010. He is a director at Galectin Therapeutics and Pieris, Mr. Prelack holds a CPA and has a B.B.A. in Finance and Accounting from the University of Massachusetts, Amherst. We believe Mr. Prelack is qualified to serve as a director based on his industry experience and service on multiple company boards.

Chau Khuong has served on Aerpio's board of directors since April 2014. Since 2003, Mr. Khuong has been a Private Equity Partner at OrbiMed Advisors. He is currently on the boards of Synlogic, Cerapedics and Inspire Medical Systems. Mr. Khuong holds a B.S. degree in Molecular, Cellular and Developmental Biology and a Master's in Public Health from Yale University. We believe that Mr. Khoung is qualified to serve as a director based on his industry experience and service on multiple company boards.

Pravin U. Dugel, M.D. has served as a member of Aerpio's board of directors since March 2017. Since 1994, Dr. Dugel has served as the Managing Partner of Retinal Consultants of Arizona and is a Founding Member of the Spectra Eye Institute. He is a Clinical Professor at the USC Roski Eye Institute, Keck School of Medicine at the University of Southern California. Dr. Dugel serves on the Advisory Board of Acucela, Inc. and as a member of the Scientific Advisory Board at MacuSight, Inc., Alcon Surgical, Genentech and Novartis. He also serves as a Member of the Medical Advisory Board at TrueVision Systems, Inc. and a Member of the Clinical Advisory Board at Opthea Limited. Dr. Dugel received his M.D. from UCLA School of Medicine and his BA from Columbia University. We believe that Dr. Dugel is qualified to serve as a director based on his industry experience and service on multiple boards.

Director Independence

Our securities are not listed on a national securities exchange or on any inter-dealer quotation system which has a requirement that a majority of directors be independent. We evaluate independence by the standards for director independence set forth in the Nasdaq Marketplace Rules. Under such rules, our board of directors has determined

that all members of the board of directors, except Stephen Hoffman and Joseph Gardner, are independent directors. Stephen Hoffman and Joseph Gardner are not independent directors under these rules because they are executive officers of our company. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our board of directors considered the association of our directors with the holders of more than 5% of our common stock. The composition and functioning of our board of directors and each of our committees complies with all applicable requirements of the Nasdaq Stock Market and the rules and regulations of the SEC. There are no family relationships among any of our directors or executive officers.

Staggered Board of Directors

In accordance with the terms of our amended and restated certificate of incorporation which became effective on April 14, 2017, our board of directors is divided into three staggered classes of directors and each is assigned to one of the three classes. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2018 for Class I directors, 2019 for Class II directors and 2020 for Class III directors.

- Our Class I directors are Paul Weiss, Caley Castelein, and Stephen Hoffman;
- Our Class II directors are Steven Prelack, Anupam Dalal and Pravin Dugel; and
- Our Class III directors are Joseph Gardner, Muneer Satter and Chau Khuong.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the number of directors shall be fixed from time to time by a resolution of a supermajority (66 2/3%) vote of the directors then in office, even if less than a quorum.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Role of Board in Risk Oversight Process

We have established a role of the chairman of the board, who is Muneer Satter and we plan to keep this role separated from the role of Chief Executive Officer. We believe that separating these positions allows our Chief Executive Officer to focus on our day-to-day business, while allowing a chairman of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our chairman, particularly as the board of directors' oversight responsibilities continue to grow. Our amended and restated by-laws and corporate governance guidelines require that our chairman of the board not be an employee an executive officer of our company, and our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations, strategic direction and intellectual property as more fully discussed in the section entitled "Risk Factors" appearing elsewhere in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees,

has responsibility for the oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of the board of directors in overseeing the management of our risks is conducted primarily through committees of the board of directors, as disclosed in the descriptions of each of the committees below and in the charters of each of the committees. The full board of directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on us, and the steps we take to manage them. When a board committee is responsible for evaluating and overseeing the management of a particular risk or risks, the chairman of the relevant committee reports on the discussion to the full board of directors during the committee reports portion of the next board meeting. This enables the board of directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.

Board Committees

As our common stock is not presently listed for trading or quotation on a national securities exchange, we are not presently required to have board committees. However, our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which operates pursuant to a charter adopted by our board of directors. The composition and functioning of all of our committees comply with all applicable requirements of the Sarbanes-Oxley Act of 2002 and SEC rules and regulations, and we intend to comply with those of the Nasdaq Stock Market.

Audit Committee

Steven Prelack, Caley Castelein and Pravin Dugel serve on the audit committee, which is chaired by Steven Prelack. Our board of directors has determined that Steven Prelack, Caley Castelein and Pravin Dugel are “independent” for audit committee purposes as that term is defined in the rules of the SEC and the applicable Nasdaq rules, and each has sufficient knowledge in financial and auditing matters to serve on the audit committee. Our board of directors has designated each of Steven Prelack and Pravin Dugel as an “audit committee financial expert,” as defined under the applicable rules of the SEC. The audit committee’s responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee’s review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;

- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and making recommendations to our board of directors regarding all such transactions; and
- reviewing quarterly earnings releases.

Compensation Committee

Anupam Dalal and Paul Weiss serve on the compensation committee, which is chaired by Anupam Dalal. Our board of directors has determined that each member of the compensation committee is "independent" as defined in the applicable Nasdaq rules. The compensation committee's responsibilities include:

- annually reviewing and recommending to the independent directors on the board of directors the corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and based on such evaluation: (i) recommending to the independent directors on the board of directors the cash compensation of our Chief Executive Officer and (ii) reviewing and recommending to the independent directors on the board of directors regarding grants and awards to our Chief Executive Officer under equity-based plans;
- reviewing and approving or recommending to the independent directors on the board of directors the cash compensation of our other executive officers;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq rules;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and recommending to the independent directors on the board of directors the compensation of our directors;
- preparing the compensation committee report required by SEC rules, if and when required, to be included in our annual proxy statement; and
- reviewing and approving the retention, termination or compensation of any consulting firm or outside advisor to assist in the evaluation of compensation matters.

Nominating and Corporate Governance Committee

Chau Khuong and Muneer Satter serve on the nominating and corporate governance committee, which is chaired by Chau Khuong. Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as defined in the applicable Nasdaq rules. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to the board of directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;

- recommending to the board of directors the persons to be nominated for election as directors and to each of the board's committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Board Diversity

Our nominating and corporate governance committee is responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individual candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- personal and professional integrity;
- ethics and values;
- experience in corporate management, such as serving as an officer or former officer of a publicly held company;
- experience in the industries in which we compete;
- experience as a director or executive officer of another publicly held company;
- diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;
- conflicts of interest; and
- practical and mature business judgment.

Our board of directors evaluates each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. The code of business conduct and ethics is available on our website at www.aerpio.com. We expect that any amendments to the code, or any waivers of its requirements, will be disclosed on our website. The reference to our web address does not constitute incorporation by reference of the information contained at or available through our website.

Limitation on Liability and Indemnification Matters

Our certificate of incorporation and bylaws contain provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Our certificate of incorporation and bylaws provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our bylaws also provide that we are obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his, her or its actions in that capacity regardless of whether we would otherwise be permitted to indemnify him, her or it under Delaware law.

In addition to the indemnification required in our certificate of incorporation (and, upon its effectiveness, our amended and restated certificate of incorporation) and bylaws, we have entered or intend to enter into indemnification agreements with each of our directors, officers and certain other employees. These agreements provide for the indemnification of our directors, officers and certain other employees for all reasonable expenses and liabilities incurred in connection with any action or proceeding brought against them by reason of the fact that they are or were our agents. We believe that these provisions in our certificate of incorporation, amended and restated certificate of incorporation, bylaws and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. This description of the limitation of liability and indemnification provisions of our certificate of incorporation, amended and restated certificate of incorporation, our bylaws and our indemnification agreements is qualified in its entirety by reference to these documents, each of which is attached as an exhibit to this prospectus.

The limitation of liability and indemnification provisions in our certificate of incorporation, amended and restated certificate of incorporation and bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors, officers or employees as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director, officer or employee.

Director Compensation

Aerpio became our wholly owned subsidiary upon the closing of the Merger on March 15, 2017. The following summarizes the compensation earned by Aerpio's non-employee directors in Aerpio's fiscal year ending December 31, 2016.

Aerpio did not pay any cash compensation to any of the non-employee members of Aerpio's board of directors, and Aerpio did not pay director fees to our directors who are Aerpio's employees. However, Aerpio reimbursed Aerpio's non-employee directors for travel and other necessary business expenses incurred in the performance of their services for Aerpio.

In 2014, Aerpio granted Dr. Dugel options to purchase Aerpio common stock, which were converted into options to purchase 16,742 shares of our common stock, having an exercise price of $1.40 per share. These options vest and become exercisable in monthly installments, subject to the individual continuing to provide services through each such vesting date.

On March 15, 2017, we adopted a compensation policy for our non-employee directors, or the Director Compensation Program. Pursuant to the Director Compensation Program, our non-employee directors will receive cash compensation, paid quarterly, as follows:

- Each non-employee director will receive an annual cash retainer in the amount of $35,000 per year.
- Any non-employee Chairman will receive an additional annual cash retainer in the amount of $25,000 per year.
- The chairperson of the audit committee will receive additional annual cash compensation in the amount of $15,000 per year for such chairperson's service on the audit committee. Each non-chairperson member of the audit committee will receive additional annual cash compensation in the amount of $7,500 per year for such member's service on the audit committee.
- The chairperson of the compensation committee will receive additional annual cash compensation in the amount of $10,000 per year for such chairperson's service on the compensation committee. Each non-chairperson member of the compensation committee will receive additional annual cash compensation in the amount of $5,000 per year for such member's service on the compensation committee.
- The chairperson of the nominating and corporate governance committee will receive additional annual cash compensation in the amount of $7,000 per year for such chairperson's service on the nominating and corporate governance committee. Each non-chairperson member of the nominating and corporate governance committee will receive additional annual cash compensation in the amount of $3,500 per year for such member's service on the nominating and corporate governance committee.

Under the Director Compensation Program, upon the director's initial appointment or election to our board of directors, each non-employee director will receive an option (the Initial Grant) to purchase that number of shares of our common stock such that the award has an aggregate grant date fair value (as defined below) equal to $181,400, rounded down to the nearest whole share (subject to adjustment as provided in the applicable equity plan). In addition, each non-employee director who has been serving as a director for the prior three months and will continue to serve as a director immediately following each annual stockholder meeting, will receive, on the date of such annual stockholder meeting, an option (the Annual Grant) to purchase that number of shares of our common stock such that the award has an aggregate grant date fair value equal to $90,700, rounded down to the nearest whole share (subject to adjustment as provided in the applicable equity plan). For purposes of the Initial Grant and the Annual Grant, "grant date fair value" will mean the fair value of an award as of the date of grant as determined in accordance with ASC Topic 718, "Share-Based Payment", using the Black-Scholes pricing model and the valuation assumptions used by the company in accounting for options as of such date of grant. The Initial Grant will vest as to one-third of the shares subject to Initial Grant on each yearly anniversary of the applicable grant date, subject to continued service through each applicable vesting date, and the Annual Grant will fully vest on the earlier of the first anniversary of the applicable grant date or the date of the next annual stockholder meeting, subject to continued service through such vesting date.

2016 Director Compensation Table

The following table sets forth information for the year ended December 31, 2016, regarding the compensation awarded to, earned by or paid to Aerpio's non-employee directors as of such date as if Aerpio been a reporting company on December 31, 2016:

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)	Total ($)
Muneer Satter	0	0	0
Paul M. Weiss	0	0	0
Anupam Dalal	0	0	0
Chau Khuong	0	0	0

Involvement in Certain Legal Proceedings

None of our directors or executive officers has been involved in any of the following events during the past 10 years:

- any bankruptcy petition filed by or against any business of which such person was a general partner or executive officer either at the time of the bankruptcy or within two years prior to that time;
- any conviction in a criminal proceeding or being subject to a pending criminal proceeding (excluding traffic violations and other minor offences);
- being subject to any order, judgment, or decree, not subsequently reversed, suspended or vacated, of any court of competent jurisdiction, permanently or temporarily enjoining, barring, suspending or otherwise limiting his or her involvement in any type of business, securities or banking activities; or
- being found by a court of competent jurisdiction (in a civil action), the Commission or the Commodity Futures Trading Commission to have violated a federal or state securities or commodities law, and the judgment has not been reversed, suspended, or vacated.

EXECUTIVE COMPENSATION

Aerpio became our wholly owned subsidiary upon the closing of the Merger on March 15, 2017. The following summarizes the compensation earned by Aerpio's executive officers named in the "Summary Compensation Table" below (referred to herein as our "named executive officers") for Aerpio's fiscal year ending December 31, 2016.

This section also discusses the material elements of Aerpio's executive compensation policies and decisions and important factors relevant to an analysis of these policies and decisions. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the information presented in the following tables and the corresponding narrative. Aerpio became our wholly-owned subsidiary upon the closing of the Merger on March 15, 2017. Unless otherwise noted, the following section is historical and has not been adjusted to give effect to the Merger or the share conversion ratio pursuant to the Merger Agreement.

Overview

Historically, Aerpio's executive compensation program has reflected its growth and corporate goals. To date, the compensation of the named executive officers has consisted of a combination of base salary, annual cash bonus, and long-term equity incentive compensation in the form of restricted stock and stock options, and other employee benefits generally available to Aerpio's employees. The named executive officers are also entitled to certain compensation and benefits upon certain terminations of employment pursuant to their executive employment agreements as described below.

The named executive officers for the year ended December 31, 2016 were as follows:

- Joseph H. Gardner, our President and Founder;
- Stephen Pakola M.D., our Chief Medical Officer;
- Kevin G. Peters M.D., our Chief Scientific Officer.

Elements of Executive Compensation

Base Salaries. Base salaries for the named executive officers are determined annually by the compensation committee, subject to review and approval by the board of directors, based on the scope of each officer's responsibilities along with his respective experience and contributions during the prior year. When reviewing base salaries, the compensation committee takes factors into account such as each officer's experience and individual performance, our performance as a whole, data from surveys of compensation paid by comparable companies, and general industry conditions, but does not assign any specific weighting to any factor.

Annual Cash Bonuses. Prior to the Merger, all of the named executive officers participated in an annual cash program sponsored by Aerpio and, following the Merger, all of the named executive officers participate in the Aerpio Pharmaceuticals, Inc. annual cash bonus program, which promotes and rewards the executives for the achievement of key strategic and business goals. In anticipation of possible fund raising activities to be completed in 2017, no bonuses were declared for 2016. The 2015 bonus plan period covers the 12-month period beginning on January 1, 2015 and ending on December 31, 2015. For the 2016 bonus plan period, the target annual bonus as a percentage of base salary, as determined based on the salary earned throughout the bonus plan period, for each of the named executive officers was up to 20%. At the beginning of the 2015 bonus plan period, the compensation committee established corporate performance goals, each having a designated weighting, which related to key development, strategic and financial goals of or company. At the end of the 2015 bonus plan period, the compensation committee met and evaluated the performance of Aerpio against the specified performance goals. Based on its evaluation, the compensation committee recommended, and the board of

directors approved, that we achieved 75% of our corporate goals. Consequently, the board of directors approved payment of cash bonuses for the 2015 bonus plan period of: $52,500 for Dr. Gardner, $48,000 for Dr. Peters, which in each case represented 75% of the named executive officer's target bonus, and $12,364 for Dr. Pakola, who joined us in October 2015.

Equity Awards. The named executive officers have historically participated in Aerpio's 2011 Plan and 2017 Plan. During fiscal year 2016, Dr. Gardner, Dr. Peters and Dr. Pakola did not receive option awards. In December 2015, Dr. Pakola received an option to purchase 390,724 shares of Aerpio common stock in connection with the commencement of his employment, which was converted to an option to purchase 167,429 shares of our common stock having an exercise price of $1.80 per share. In 2012 and 2014, Aerpio granted Dr. Gardner options to purchase Aerpio common stock, which were converted into options to purchase 27,727 and 207,628 shares of our common stock respectively, each having an exercise price of $1.65 and $2.10 per share respectively. In 2011, 2013, and 2014, Aerpio also granted Dr. Gardner shares of Aerpio restricted common stock which were converted into 32,231, 113,225, 175,473 shares of our restricted common stock respectively. These shares of restricted stock vest in monthly installments, subject to Dr. Gardner continuing to provide services through each such vesting date. After the Merger, in 2017, we granted Dr. Hoffman an option to purchase 586,012 shares of our common stock, having an exercise price of $5.50 per share. Also after the Merger, in 2017, we granted Mr. Rogers an option to purchase 293,006 shares of our common stock, having an exercise price of $5.50 per share. These options vest 25% on the first anniversary of the vesting commencement date and then in 36 monthly installments thereafter, subject to Mr. Rogers continuing to provide services through each such vesting date. Finally, after the Merger, in 2017, we granted Dr. Gardner an option to purchase 135,000 shares of our common stock, having an exercise price of $5.50 per share, which option shall vest in full on July 1, 2018, subject to Dr. Gardner continuing to provide services through such vesting date.

Other Benefits. Our named executive officers are eligible for additional benefits, such as participation in our 401(k) plan, our employee stock purchase plan and basic health benefits that are generally available to all of our employees.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of the named executive officers for the periods ending December 31, 2016 and 2015.

Name and Principal Position	Year	Salary ($)	Non-Equity Incentive Compensation ($)(1)	Option Awards ($)(2)	All Other Compensation ($)(3)	Total ($)
Joseph Gardner	2016	350,000	—	—	1,069	351,069
President and Founder	2015	350,000	52,500	—	1,069	403,569
Kevin G. Peters	2016	320,000	—	—	1,069	321,069
Chief Scientific Officer	2015	320,000	48,000	—	697	368,697
Stephen Pakola	2016	340,000	—	—	243	340,243
Chief Medical Officer	2015	82,424(4)	12,364	204,739	41	299,568

(1) No bonuses were declared for 2016. Amounts for 2015 represent cash bonuses earned for the 12-month bonus plan period from January 1, to December 31, 2015.

(2) The amounts reported in the Option Awards column granted to the named executive officers represent the fair value of the stock options as of the grant date as computed in accordance with FASB ASC Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in the Option Awards column are set forth in Note 8 to our financial statements for the year ended December 31, 2016 and 2015. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options. The amounts reported in the Stock Awards

column granted to the named executive officers represent the fair value of the stock awards as determined by our board of directors, with input from management and third party valuation experts.

(3) Amounts represent the dollar value of life insurance premiums paid by us on behalf of the named executive officers.

(4) Dr. Pakola joined Aerpio in October 2015, with an annual base salary of $340,000. The amount in the table reflects his partial year of service for 2015.

In addition, after the Merger, in November 2017, Michael Rogers joined as our Chief Financial Officer. Pursuant to his employment agreement, Mr. Rogers is entitled to an annual base salary of $375,000 and an annual performance bonus targeted at 40% of his base salary. Furthermore, after the Merger, in December 2017, Stephen Hoffman joined as our Chief Executive Officer. Pursuant to his employment agreement, Dr. Hoffman is entitled to an annual base salary of $470,000 and an annual performance bonus targeted at 50% of his base salary.

Outstanding Equity Awards at Fiscal Year-End 2016

The following table sets forth information concerning outstanding equity awards for each of the named executive officers as of December 31, 2016 and the numbers below have not been adjusted to give effect to the Merger or the share conversion ratio pursuant to the Merger Agreement:

	Option Awards					Stock Awards	
Name and Principal Position	Vesting Commencement Date(1)	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Securities That Have Not Vested (#)	Market Value of Securities That Have Not Vested ($)
Joseph Gardner	3/22/2012	64,706	—	$ 0.71	3/21/2022	—	$ —
President and Founder	2/18/2014	353,305	131,228	$ 0.90	2/17/2024	—	$ —
	10/23/2014					179,154	$ 168,405
Kevin G. Peters	3/22/2012	4,464	—	$ 0.71	3/21/2022	—	—
Chief Scientific Officer	2/18/2014					49,314	$ 17,260
	10/23/2014					97,058	$ 91,235
Stephen Pakola	12/29/2015	113,961	276,763(2)	$ 0.77	12/27/2025	—	—
Chief Medical Officer							

(1) Except as otherwise noted, options vest and become exercisable in 48 equal installments on each monthly anniversary of the vesting commencement date, such that all awards will be vested on the fourth anniversary of the vesting commencement date, subject to the holder continuing to provide services to the company through such vesting date.

(2) Vests 25% on the first anniversary of the vesting commencement date, then vests in 36 equal monthly installments thereafter, such that the option is vested on the fourth anniversary of the vesting commencement date, subject to the holder continuing to provide services to the company through such vesting date.

Employment Agreements

We have entered into employment agreements with each of our named executive officers and our other executive officers. Each employment agreement provides for “at will” employment, meaning that either we or the officer may terminate the employment relationship at any time without cause.

Executive Employment Agreement with Joseph H. Gardner. Dr. Gardner’s base salary under his employment agreement, as amended after the Merger, is $410,000, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus with a target amount equal to 50% of his base salary. Dr. Gardner is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Dr. Gardner's employment agreement, as amended after the Merger, provides that, in the event that (a) prior to July 1, 2018 his employment is terminated by us for reasons other than "cause" (as defined in his employment agreement, as amended) or he remains an employee through July 1, 2018 and his employment is terminated by us without cause or he resigns for "good reason" (as defined in his employment agreement, as amended) thereafter,, and subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) an amount equal to twelve months of his base salary, (ii) if Dr. Gardner is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of twelve months following termination or the end of Dr. Gardner's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to Dr. Gardner had he remained employed with us, and (iii) acceleration of all time-based equity awards held by Dr. Gardner in which Dr. Gardner would have vested if he had remained employed for an additional twelve months or (b) Dr. Gardner resigns for "good reason" prior to July 1, 2018 and subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) an amount equal to nine months of his base salary, (ii) if Dr. Gardner is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of nine months following termination or the end of Dr. Gardner's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to Dr. Gardner had he remained employed with us, and (iii) acceleration of all time-based equity awards held by Dr. Gardner in which Dr. Gardner would have vested if he had remained employed for an additional six months. All amounts payable to Dr. Gardner shall be made in substantially equal installments over nine months following his termination, except that, in the case of a termination that occurs after July 1, 2018, such amount shall be paid in a lump sum.

In lieu of the payments and benefits described in the preceding paragraph, in the event that Dr. Gardner's employment is terminated by us without cause or Dr. Gardner resigns for good reason, in either case within 12 months following a "change in control" (as defined in his employment agreement, as amended), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) a lump sum cash payment equal to 0.75 times the sum of (x) Dr. Gardner's then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) and (y) his target annual incentive compensation, (ii) if Dr. Gardner is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of nine months following termination or the end of Dr. Gardner's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us and (iii) full acceleration of all time-based equity awards held by Dr. Gardner.

In addition, Dr. Gardner remains bound by certain restrictive covenants, including non-competition and non-solicitation provisions, which have been incorporated by reference into the employment agreement from his prior employment agreement. These restrictive covenants apply during the term of Dr. Gardner's employment and for one year thereafter.

Executive Employment Agreement with Kevin G. Peters. Dr. Peters' base salary under his employment agreement is $329,600, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus with a target amount equal to 20% of his base salary. Dr. Peters is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Dr. Peters' employment agreement provides that, in the event that his employment is terminated by us without "cause" (as defined in his employment agreement) or Dr. Peters resigns for "good reason" (as defined in his employment agreement) subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) an amount equal to six months of his base salary, (ii) if Dr. Peters is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of six months following termination or the end of Dr. Peters' COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to Dr. Peters had he remained employed with us, and (iii) acceleration of all time-based equity awards held by

Dr. Peters in which Dr. Peters would have vested if he had remained employed for an additional six months. All amounts payable to Dr. Peters shall be made in substantially equal installments over six months following his termination.

In lieu of the payments and benefits described in the preceding paragraph, in the event that Dr. Peters' employment is terminated by us without cause or Dr. Peters resigns for good reason, in either case within 12 months following a "change in control" (as defined in his employment agreement), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) a lump sum cash payment equal to 0.5 times the sum of (x) Dr. Peters' then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) and (y) his target annual incentive compensation, (ii) if Dr. Peters is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of six months following termination or the end of Dr. Peters' COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us and (iii) full acceleration of all time-based equity awards held by Dr. Peters.

In addition, Dr. Peters remains bound by certain restrictive covenants, including non-competition and non-solicitation provisions, which have been incorporated by reference into the new employment agreement from his prior employment agreement. These restrictive covenants apply during the term of Dr. Peters' employment and for one year thereafter.

Executive Employment Agreement with Stephen Pakola, M.D. Dr. Pakola's base salary under his employment agreement is $350,200, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus with a target amount equal to 20% of his base salary. Dr. Pakola is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Dr. Pakola's employment agreement provides that, in the event that his employment is terminated by us without "cause" (as defined in his new employment agreement) or Dr. Pakola resigns for "good reason" (as defined in his employment agreement) subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) an amount equal to six months of his base salary, (ii) if Dr. Pakola is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of six months following termination or the end of Dr. Pakola's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to Dr. Pakola had he remained employed with us, and (iii) acceleration of all time-based equity awards held by Dr. Pakola in which Dr. Pakola would have vested if he had remained employed for an additional six months. All amounts payable to Dr. Pakola shall be made in substantially equal installments over six months following his termination.

In lieu of the payments and benefits described in the preceding paragraph, in the event that Dr. Pakola's employment is terminated by us without cause or Dr. Pakola resigns for good reason, in either case within 12 months following a "change in control" (as defined in his employment agreement), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) a lump sum cash payment equal to 0.5 times the sum of (x) Dr. Pakola's then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) and (y) his target annual incentive compensation, (ii) if Dr. Pakola is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of six months following termination or the end of Dr. Pakola's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us and (iii) full acceleration of all time-based equity awards held by Dr. Pakola.

In addition, Dr. Pakola has also entered into an employee confidentiality and assignment agreement with us that also contains certain restrictive covenants, including non-competition and non-solicitation provisions that apply during the term of Dr. Pakola's employment and for one year thereafter.

Executive Employment Agreement with Stephen Hoffman. Dr. Hoffman's initial base salary under his employment agreement is $470,000, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus with a target amount equal to 50% of his base salary. Dr. Hoffman is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Dr. Hoffman's employment agreement provides that, in the event that his employment is terminated by us without "cause" (as defined in his employment agreement) or Dr. Hoffman resigns for "good reason" (as defined in his employment agreement) subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) an amount equal to twelve months of his base salary, (ii) if Dr. Hoffman is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of twelve months following termination or the end of Dr. Hoffman's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to Dr. Hoffman had he remained employed with us, and (iii) acceleration of all time-based equity awards held by Dr. Hoffman in which Dr. Hoffman would have vested if he had remained employed for an additional twelve months. All amounts payable to Dr. Hoffman shall be made in substantially equal installments over twelve months following his termination.

In lieu of the payments and benefits described in the preceding paragraph, in the event that Dr. Hoffman's employment is terminated by us without cause or Dr. Hoffman resigns for good reason, in either case within fifteen months following a "change in control" (as defined in his employment agreement), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) a lump sum cash payment equal to 1.5 times the sum of (x) Dr. Hoffman's then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) and (y) his target annual incentive compensation, (ii) if Dr. Hoffman is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of twelve months following termination or the end of Dr. Hoffman's COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us and (iii) acceleration of all time-based equity awards held by Dr. Hoffman in which Dr. Hoffman would have vested if he had remained employed for an additional twelve months.

In addition, Dr. Hoffman remains bound by certain restrictive covenants, including non-competition and non-solicitation provisions. These restrictive covenants apply during the term of Dr. Hoffman's employment and for one year thereafter.

Executive Employment Agreement with Michael Rogers. Mr. Rogers' initial base salary under his employment agreement is $375,000, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus with a target amount equal to 40% of his base salary. Mr. Rogers is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

Mr. Rogers' employment agreement provides that, in the event that his employment is terminated by us without "cause" (as defined in his employment agreement) or Mr. Rogers resigns for "good reason" (as defined in his employment agreement) subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) an amount equal to twelve months of his base salary, (ii) if Mr. Rogers is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of twelve months following termination or the end of Mr. Rogers' COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to Mr. Rogers had he remained employed with us, and (iii) acceleration of all time-based equity awards held by Mr. Rogers in which Mr. Rogers would have vested if he had remained employed for an additional twelve months. All amounts payable to Mr. Rogers shall be made in substantially equal installments over twelve months following his termination.

In lieu of the payments and benefits described in the preceding paragraph, in the event that Mr. Rogers' employment is terminated by us without cause or Mr. Rogers resigns for good reason, in either case within

12 months following a “change in control” (as defined in his employment agreement), subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) a lump sum cash payment equal to 1 times the sum of (x) Mr. Rogers’ then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) and (y) his target annual incentive compensation, (ii) if Mr. Rogers is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of six months following termination or the end of Mr. Rogers’ COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us and (iii) full acceleration of all time-based equity awards held by Mr. Rogers.

In addition, Mr. Rogers remains bound by certain restrictive covenants, including non-competition and non-solicitation provisions, which have been incorporated by reference into the new employment agreement from his prior employment agreement. These restrictive covenants apply during the term of Mr. Rogers’ employment and for one year thereafter.

Employee Benefit Plans

2017 Stock Option and Incentive Plan

On March 3, 2017, our board of directors adopted, and on March 10, 2017, our stockholders approved, our 2017 Stock Option and Incentive Plan, or the 2017 Plan, which became effective on April 14, 2017. The 2017 Plan replaced our 2011 Equity Incentive Plan, or the 2011 Plan, as our board of directors has determined not to make additional awards under the 2011 Plan. Our 2017 Plan provides flexibility to our compensation committee to use various equity-based incentive awards as compensation tools to motivate our workforce.

We initially reserved 4,600,000 shares of our common stock, less the number of shares subject to issued and outstanding awards under the 2011 Plan that were assumed in the Merger, or the Initial Limit, for the issuance of awards under the 2017 Plan. The 2017 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2018, by 4% of the outstanding number of shares of our common stock on the immediately preceding December 31, or such lesser number of shares as determined by our board of directors, or the Annual Increase. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2017 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of stock, expire or are otherwise terminated (other than by exercise) under the 2017 Plan will be added back to the shares of common stock available for issuance under the 2017 Plan.

Stock options and stock appreciation rights with respect to no more than 4,600,000 shares of stock may be granted to any one individual in any one calendar year. The maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the Initial Limit cumulatively increased on January 1, 2018 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 4,600,000 shares of common stock.

The 2017 Plan is administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2017 Plan. Persons eligible to participate in the 2017 Plan will be those full or part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation and committee in its discretion.

The 2017 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code, or the Code, and options that do not so qualify.

The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of the common stock on the date of grant.

Our compensation committee may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2017 Plan. Unrestricted stock may be granted to participants in recognition of past services or other valid consideration and may be issued in lieu of cash compensation due to such participant. Our compensation committee may grant cash bonuses under the 2017 Plan to participants, subject to the achievement of certain performance goals.

Our compensation committee may grant awards of restricted stock, restricted stock units or stock- or cash-based awards under the 2017 Plan that are intended to qualify as “performance-based compensation” under Section 162(m) of the Code. Those awards would only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that would be used with respect to any such awards include: total shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common stock, economic value-added, funds from operations or similar measure, sales or revenue, development, clinical or regulatory milestones, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group. From and after the time that we become subject to Section 162(m) of the Code, the maximum award that is intended to qualify as “performance-based compensation” under Section 162(m) of the Code that may be made to any one employee during any one calendar year is 4,600,000 shares of common stock with respect to a stock-based award and $2,000,000 with respect to a cash-based award.

The 2017 Plan provides that in the case of, and subject to, the consummation of a “sale event” (as defined in the 2017 Plan), all outstanding awards may be assumed, substituted or otherwise continued by the successor entity. To the extent that the successor entity does not assume, substitute or otherwise continue such awards, then (i) all stock options and stock appreciation rights will automatically become fully exercisable and the restrictions and conditions on all other awards with time-based conditions will automatically be deemed waived, and awards with conditions and restrictions relating to the attainment of performance goals may become vested and non-forfeitable in connection with a sale event in the compensation committee’s discretion and (ii) upon the effectiveness of the sale event, the 2017 Plan and all awards will automatically terminate. In the event of such termination, (i) individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights (to the extent exercisable) prior to the sale event; or (ii) we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights (to the extent then exercisable).

Our board of directors may amend or discontinue the 2017 Plan and our compensation committee may amend the exercise price of options and amend or cancel outstanding awards for purposes of satisfying changes in law or

any other lawful purpose but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2017 Plan require the approval of our stockholders. No awards may be granted under the 2017 Plan after the date that is 10 years from the date of stockholder approval. No awards under the 2017 Plan have been made prior to the date of this Form 8-K.

2011 Equity Incentive Plan

The 2011 Equity Incentive Plan, or the 2011 Plan, was approved by Aerpio's board of directors and Aerpio's stockholders on December 22, 2011, and was most recently amended in April 2014, and was assumed by us upon the Merger. Aerpio had reserved an aggregate of 5,860,874 shares of Aerpio's common stock for the issuance of options and other equity awards under the 2011 Plan. After we assumed the 2011 Plan, options to purchase 927,592 shares of our common stock were outstanding under the 2011 Plan at a weighted average exercise price of $1.69 per share and no shares remained available for future grant under the 2011 Plan. Effective upon the closing of the Merger, our board of directors has determined not to grant any further awards under our 2011 Plan, but all outstanding awards under the 2011 Plan will continue to be governed by their existing terms. The shares to be issued under options we assumed that were issued under the 2011 Plan will be authorized but unissued shares or shares we reacquire.

The 2011 Plan is administered by our board of directors. The board of directors or a committee appointed by the board has the authority to select the individuals to whom awards will be granted, to make any combination of awards to participants and to determine the specific terms and conditions of each award.

The option exercise price of each option issued under the 2011 Plan was determined by our board of directors but was not less than 100% of the fair market value of Aerpio's common stock on the date of grant. In the case of an incentive stock option granted to a participant who, at the time of grant of such option, owned stock representing more than 10% of the voting power of all classes of our stock, then the exercise price was not less than 110% of the fair market value of the Aerpio's common stock on the date of grant. The term of each option was fixed by the board of directors and did not exceed 10 years from the date of grant.

The 2011 Plan provides that upon the occurrence of a "corporate transaction" as defined in the 2011 Plan, awards may be assumed, substituted for new awards of a successor entity, or otherwise terminated at the effective time of such corporate transaction. In the case of the termination of all outstanding options, such options may be exercised to the extent then exercisable within a period of time prior to the consummation of the corporate transaction. In the case of restricted stock or stock bonuses, the unvested portion of such awards will terminate in exchange for a cash payment in amount equal to the product of the per share cash consideration and the number of shares subject to each such award. Our board of directors may also provide alternative consideration for any outstanding awards that it determines to be equitable in the circumstances, including cash.

Our board of directors may amend or terminate the 2011 Plan at any time, subject to stockholder approval where such approval is required by applicable law, provided that no such action may materially and adversely affect any of the rights of a participant under any awards previously granted without his or her written consent. The board of directors has determined not to make any further grants under the 2011 Plan as of the Effective Time of the Merger.

Employee Stock Purchase Plan

On March 3, 2017 our board of directors adopted, and on March 10, 2017, our stockholders approved, our 2017 Employee Stock Purchase Plan, or the ESPP, which became effective on April 14, 2017 and was amended and restated on December 14, 2017, subject to approval by shareholders. The ESPP authorizes the issuance of up to a total of 300,000 shares of common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance under the ESPP shall be cumulatively increased each January 1, beginning on January 1, 2018, by the lesser of (i) 1% of the outstanding number of shares of our common stock

on the immediately preceding December 31, (ii) 350,000 shares, or (ii) such lesser number of shares as determined by our board of directors. The number of shares reserved and available for issuance under the ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees who we have employed for at least 30 days and whose customary employment is for more than 20 hours a week are eligible to participate in the ESPP. Any employee who owns five percent or more of the voting power or value of our shares of common stock is not eligible to purchase shares under the ESPP.

We may make one or more offerings each year to our employees to purchase shares under the ESPP. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 business days before the relevant offering date.

Each employee who is a participant in the ESPP may purchase shares by authorizing payroll deductions of up to one percent of his or her base compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase shares of common stock on the last business day of the offering period at a price equal to 85 percent of the fair market value of the common stock on the first business day or the last business day of the offering period, whichever is lower, subject to the limits set forth in the ESPP with respect to the number of shares of common stock that may be purchased by any one employee during each offering period. Under applicable tax rules, an employee may purchase no more than $25,000 worth of common stock, valued at the start of the purchase period, under the ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

The ESPP may be terminated or amended by our board of directors at any time. An amendment that increases the number of shares of common stock that are authorized under the ESPP and certain other amendments require the approval of our stockholders.

Senior Executive Cash Incentive Bonus Plan

On March 15, 2017, our board of directors adopted the Aerpio Pharmaceuticals, Inc. Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or corporate performance goals, as well as individual performance objectives.

Our compensation committee may select corporate performance goals from among the following: cash flow (including, but not limited to, operating cash flow and free cash flow); revenue; corporate revenue; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of our common stock; economic value-added; development, clinical, regulatory or commercial milestones; acquisitions or strategic transactions; operating income (loss); return on capital, assets, equity, or investment; stockholder returns; return on sales; gross or net profit levels; productivity; expense efficiency; margins; operating efficiency; customer satisfaction; working capital; earnings (loss) per share of our common stock; bookings, new bookings or renewals; sales or market shares; number of customers, number of new customers or customer references; operating income and/or net annual recurring revenue, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, as compared to results of a peer group, against the market as a whole or applicable market, indices and/or on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the governance

committee and communicated to each executive. The corporate performance goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. Subject to the rights contained in any agreement between the executive officer and us, an executive officer must be employed by us on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion.

Retirement Plan

We offer a 401(k) plan to eligible employees, including our named executive officers. In accordance with this plan, all eligible employees may contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary. We made no contributions during the year ended December 31, 2016. We intend for the 401(k) plan to qualify, depending on the employee's election, under Section 401(a) of the Code, so that contributions by employees, and income earned on those contributions, are not taxable to employees until withdrawn from the 401(k) plan.

Indemnification of Officers and Directors

We have agreed to indemnify our directors and executive officers in certain circumstances. See *"Directors, Executive Officers, Promoters and Control Persons—Limitation on Liability and Indemnification Matters."*

Compensation Consultant As a part of determining compensation for our named executive officers, the compensation committee has engaged Radford, a business unit of Aon plc, as an independent compensation consultant. Radford provides analysis and recommendations to the compensation committee regarding:

- trends and emerging topics with respect to executive compensation;
- peer group selection for executive compensation benchmarking;
- compensation practices of our peer group;
- compensation programs for executives and all of our employees; and
- stock utilization and related metrics.

When requested, Radford consultants attend meetings of the compensation committee, including executive sessions in which executive compensation issues are discussed. Radford reports to the compensation committee and not to management, although Radford meets with management for purposes of gathering information for its analyses and recommendations.

In determining to engage Radford, the compensation committee considered the independence of Radford taking into consideration relevant factors, including the absence of other services provided to us by Radford, the amount of fees we paid to Radford as a percentage of Radford's total revenue, the policies and procedures of Radford that are designed to prevent conflicts of interest, any business or personal relationship of the individual compensation advisors employed by Radford with any of our executive officers, any business or personal relationship the individual compensation advisors employed by Radford have with any member of the compensation committee, and any shares of our stock owned by Radford or the individual compensation advisors employed by Radford. The compensation committee has determined, based on its analysis in light of all relevant factors, including the factors listed above, that the work of Radford and the individual compensation advisors employed by Radford as compensation consultants to the compensation committee has not created any conflicts of interest, and that Radford is independent pursuant to the independence standards set forth in the Nasdaq Stock Market listing standards promulgated pursuant to Section 10C of the Exchange Act.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

SEC rules require us to disclose any transaction or currently proposed transaction in which we were a participant and in which any related person has or will have a direct or indirect material interest involving the lesser of $120,000 or 1% of the average of our total assets as of the end of last two completed fiscal years. A related person is any executive officer, director, nominee for director, or holder of 5% or more of our common stock, or an immediate family member of any of those persons.

The following is a description of transactions since January 1, 2014 to which we have been a party, in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or holders of more than 5% of Aerpio's pre-Merger capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described in the section titled "Executive Compensation." The following description is historical and has not been adjusted to give effect to the Merger or the share conversion ratio pursuant to the Merger Agreement.

Sales and Purchases of Securities

Sales of Series A2 Preferred Stock

In April 2014, Aerpio issued an aggregate of 10,476,182 shares of Series A2 convertible preferred stock at a price per share of $2.10 for aggregate gross consideration of approximately $22 million to 37 accredited investors. The table below sets forth the number of shares of Series A2 convertible preferred stock sold to our directors, executive officers or holders of more than 5% of Aerpio's pre-Merger capital stock, or an affiliate or immediate family member thereof. Each outstanding 2.3336572 shares of Aerpio's Series A2 convertible preferred stock was converted into one share of our common stock in connection with the Merger.

Purchasers	Shares of Series A2 Preferred Stock	Aggregate Purchase Price
Joseph Gardner	44,043	$ 92,491.26
Entities affiliated with Kearny Venture(1)	349,749	$ 734,474.87
Novartis Bioventures Ltd.	1,585,609	$ 3,329,780.14
Trusts and Other Entities affiliated with Muneer A. Satter(2)	519,973	$ 1,091,943.34
Triathlon Medical Ventures	65,264	$ 137,055.70
Venture Investors Early Stage Fund IV	139,598	$ 293,156.50
OrbiMed Private Investments V, L.P.	7,142,857	$14,999,999.70

(1) Consists of 342,757 shares held by Kearny Venture Partners, L.P. and 6,992 shares held by Kearny Venture Partners Entrepreneurs Fund, L.P.

(2) Consists of (a) 285,073 shares of Series A2 convertible preferred stock that are held by the Muneer A. Satter Revocable Trust for which Muneer A. Satter serves as trustee and, in such capacity, has sole voting and dispositive power over all such shares and (b) 234,900 shares Series A2 convertible preferred stock that are held by various other trusts and other entities for which Muneer A. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive power over all such shares.

Convertible Promissory Note Purchase Agreement

In March, April and July 2016, Aerpio issued convertible promissory notes for an aggregate principal amount of approximately $9 million to 54 accredited investors. The Convertible Notes accrued interest at 8% per annum, compounded annually. There was approximately $437,000 of accrued interest outstanding as of December 31, 2016. All outstanding principal and interest under these Spring 2016 Notes converted into shares of Aerpio common stock immediately prior to the Merger, which were then converted into shares of our common stock on

a 2.3336572:1 basis at the effective time of the Merger. The table below sets forth the principal amount of the convertible promissory notes sold to our directors, executive officers or holders of more than 5% of Aerpio's pre-Merger capital stock, or an affiliate or immediate family member thereof.

	Aggregate Principal Price
Joseph Gardner	$ 89,664.26
Entities affiliated with Kearny Venture(1)	$ 680,312.16
Entities affiliated with Novartis Bioventures Ltd.(2)	$ 2,788,558.02
Trusts and Other Entities affiliated with Muneer A. Satter(3)	$ 1,127,983.60
Triathlon Medical Ventures	$ 439,298.86
Venture Investors Early Stage Fund IV	$ 693,140.72
OrbiMed Private Investments V, L.P.	$ 1,942,191.32

(1) Consists of an aggregate principal price of (a) $627,011.90 by Kearny Venture Partners, L.P., (b) $12,788.60 by Kearny Venture Partners Entrepreneurs Fund, L.P., (c) $36,320.76 by Revelation TWHVP, LLC, and (d) $4,190.90 by TWHVP SPV, LLC.

(2) Consists of an aggregate principal price of $2,788,558.02 held by Novartis International Pharmaceutical Investment Ltd., an entity affiliated with Novartis Bioventures Ltd.

(3) Consists of an aggregate principal price of (a) $521,039.22 by the Muneer A. Satter Revocable Trust for which Muneer A. Satter serves as trustee and, in such capacity, has sole voting and dispositive power over all such amount and (b) $606,944.38 by various other trusts and other entities for which Muneer A. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive power over all such amount.

Convertible Promissory Note Purchase Agreement

In October 2016 and January 2017, Aerpio issued convertible promissory notes for an aggregate principal amount of approximately $3.8 million to 53 accredited investors. The Convertible Notes accrued interest at 8% per annum, compounded annually. There was approximately $46,000 of accrued interest outstanding as of December 31, 2016. All outstanding principal and interest under these Winter 2016 Notes converted into shares of Aerpio common stock immediately prior to the Merger, which were then converted into shares of our common stock on a 2.3336572:1 basis at the effective time of the Merger. The table below sets forth the principal amount of the convertible promissory notes sold to our directors, executive officers or holders of more than 5% of Aerpio's pre-Merger capital stock, or an affiliate or immediate family member thereof.

Purchasers	Aggregate Principal Price
Joseph Gardner	$ 37,553.38
Entities affiliated with Kearny Venture(1)	$ 284,929.84
Entities affiliated with Novartis Bioventures Ltd.(2)	$ 1,167,910.04
Trusts and Other Entities affiliated with Muneer A. Satter(3)	$ 472,424.59
Triathlon Medical Ventures	$ 183,988.12
Venture Investors Early Stage Fund IV	$ 290,302.73
OrbiMed Private Investments V, L.P.	$ 813,432.86

(1) Consists of an aggregate principal price of (a) $262,606.51 by Kearny Venture Partners, L.P. (b) $5,356.15 by Kearny Venture Partners Entrepreneurs Fund, L.P., (c) $15,211.94 by Revelation TWHVP, LLC, and (d) $1,755.24 by TWHVP SPV, LLC.

(2) Consists of an aggregate principal price of $1,167,910.04 held by Novartis International Pharmaceutical Investment Ltd., an entity affiliated with Novartis Bioventures Ltd.

(3) Consists of an aggregate principal price of (a) $200,994.68 by the Muneer A. Satter Revocable Trust for which Muneer A. Satter serves as trustee and, in such capacity, has sole voting and dispositive power over all such amount and (b) $271,429.91 by various other trusts and other entities for which Muneer A. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive power over all such amount.

Participation in the Offering

Certain of our existing investors, including investors affiliated with certain of our directors, have purchased an aggregate of 3,512,955 shares of our common stock in the Offering, for an aggregate purchase price of $17,564,788. Such purchases were made on the same terms as the shares that were sold to other investors in the Offering and not pursuant to any pre-existing contractual rights or obligations.

Indemnification Agreements and Directors' and Officers' Liability Insurance

We have entered into indemnification agreements with each of our directors and executive officers. These agreements, among other things, require us to indemnify each director and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Employment Agreements and Offer Letters

Each of our executive officers is employed with us under the terms of their employment agreement or offer letter, as applicable. For more information regarding these employment agreements for Messrs. Gardner, Peters, Pakola, Hoffman and Rogers, see the section titled "*Executive Compensation—Narrative to Summary Compensation Table and Outstanding Equity Awards at 2016 Year End*."

Other Transactions

We have granted stock options to our executive officers. For a description of these stock options granted to such individuals, see the section titled "*Executive Compensation*." We have also granted stock options to certain members of the board of directors, and will do so in the future pursuant to our non-employee director compensation policy. For a description of these stock options, see the section titled "*Management—Director Compensation Table*."

Policies and Procedures for Related-Person Transactions

Our board of directors has adopted a written related-person transaction policy setting forth the policies and procedures for the review and approval or ratification of related-person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's-length transaction and the extent of the related person's interest in the transaction. Furthermore, all related-person transactions with a majority stockholder requires a supermajority (66 2/3%) vote of the directors then in office. All of the transactions described in this section occurred prior to the adoption of this policy.

SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table sets forth information relating to the beneficial ownership of our common stock at December 31, 2017, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of the outstanding shares of our common stock;
- each of our directors;
- each of our named executive officers; and
- all current directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of December 31, 2017 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by such person.

The percentage of shares beneficially owned is computed on the basis of 27,070,038 shares of common stock outstanding as of December 31, 2017. Shares of common stock that a person has the right to acquire within 60 days of December 31, 2017 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed in the table is c/o Aerpio Pharmaceuticals, Inc., 9987 Carver Road, Suite 420, Cincinnati, Ohio 45242.

	Shares Beneficially Owned	
	Number	Percentage
5% Stockholders:		
Novartis Bioventures Ltd.(1)	5,805,550	21.4%
Entities Affiliated with OrbiMed Private Investments III, LP(2)	4,416,446	16.3%
Trusts and Other Entities Affiliated with Muneer A. Satter(3)	3,241,835	12.0%
Venture Investors Early Stage Fund IV(4)	1,576,167	5.8%
Kearny Venture Partners, L.P. and related funds(5)	1,603,526	5.9%
Named Executive Officers, Other Executive Officers and Directors:		
Muneer A. Satter(3)	3,241,835	12.0%
Chau Khuong(2)	4,416,446	16.3%
Steven Prelack	—	*
Paul Weiss(4)	1,576,167	5.8%
Caley Castelein(5)	1,603,526	5.9%
Anupam Dalal(6)	76,204	*
Pravin Dugel(7)	14,268	*
Joseph Gardner(8)	828,374	3.0%
Kevin Peters(9)	322,448	1.2%
Steve Pakola(10)	101,153	*
Stephen Hoffman	—	*
Michael Rogers	—	*
All directors and executive officers as a group (12 persons)	12,180,421	44.4%

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

(1) Consists of 5,805,550 shares of common stock owned directly by Novartis Bioventures, Ltd. The board of directors of Novartis Bioventures Ltd. has sole voting and investment control and power over such shares. None of the members of its board of directors has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares. Novartis Bioventures Ltd. is an indirectly-owned subsidiary of Novartis AG. The address of Novartis Bioventures Ltd. is 131 Front Street, Hamilton, HM12, Bermuda.

(2) Consists of 4,416,446 shares of common stock owned directly by OrbiMed Private Investments III, LP, or OPI III. OrbiMed Advisors LLC, or OrbiMed, is the managing member of GP III, which is the general partner of OPI III. Samuel D. Isaly is the managing member of and owner of a controlling interest in OrbiMed. By virtue of such relationships, GP III, OrbiMed and Mr. Isaly may be deemed to have voting and investment power over the shares held by OPI III and as a result may be deemed to have beneficial ownership of such shares. Chau Khuong, an employee of OrbiMed, is a member of our board of directors. Each of GP III, OrbiMed, Mr. Isaly and Mr. Khuong disclaims beneficial ownership of the shares held by OPI III, except to the extent of its or his pecuniary interest therein, if any. The address of OrbiMed Investments and OrbiMed Associates is c/o OrbiMed Advisors LLC, 601 Lexington Avenue, 54th Floor, New York, New York 10022.

(3) Consists of (a) 976,568 shares of common stock that are held by the Muneer A. Satter Revocable Trust for which Muneer A. Satter serves as trustee and, in such capacity, has sole voting and dispositive power over all such shares, (b) 1,145,267 shares of common stock that are held by various other trusts and other entities for which Muneer A. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive power over all such shares (collectively, the “Satter Investors”), and (c) 1,120,000 shares of common stock that are held by Satter Medical Technology Partners, L.P., or SMTP, and Muneer A. Satter has sole voting and dispositive power over all such shares. The address of the Satter Investors and SMTP is c/o Satter Management Co., L.P., 676 North Michigan Avenue, Suite 4000, Chicago, Illinois 60610.

(4) Consists of 1,576,475 shares of common stock owned directly by Venture Investors Early Stage Fund IV Limited Partnership, or VIESF. The general partner of VIESF, VIESF IV GP LLC, has sole voting and investment control over the shares owned by VIESF. The members of VIESF IV GP LLC, John Neis, Paul M. Weiss, Scott Button, George Arida, James R. Adox, Loren G. Peterson, and Venture Investors Southeast LLC (of which Roger H. Ganser is the sole member), have sole voting and investment power for VIESF IV GP LLC with respect to its voting power in its capacity as General Partner for the shares held by VIESF. None of the members of VIESF IV GP LLC has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of Venture Investors Early Stage Fund IV Limited Partnership is 505 South Rosa Road, Suite 201, Madison, Wisconsin, 53719.

(5) Consists of (i) 1,571,475 shares of common stock owned directly by Kearny Venture Partners, L.P., or KVP and (ii) 32,051 shares of common stock owned directly by Kearny Venture Partners Entrepreneurs Fund, L.P., or KVPE. The general partner of both KVP and KVPE is Kearny Venture Associates, L.L.C., or KVA. KVA has the sole voting and investment control over the shares owned by KVP and KVPE, and the Managing Members of KVA share in the voting and investment control over such shares controlled by KVA. The Managing Members of KVA are Caley Castelein, Richard Spalding and James Shapiro. None of the Managing Members of KVA has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of KVA is One Embarcadero, Suite 3700, San Francisco, CA 94111.

(6) Consists of (i) 7,882 shares of common stock owned directly by TWHVP SPV, LLC, or TWHVP, and (ii) 68,322 shares of common stock owned directly by Revelation TWHVP, LLC, or Revelation. The general partner of TWHVP and Revelation is Kearny Venture Associates II, LLC or KVA II. KVA II has the sole voting and investment control over the shares owned by TWHVP and Revelation, and the Managing Members of KVA II have sole voting and investment control over the shares controlled by KVA II. The Managing Members of KVA II are Caley Castelein, Anupam Dalal and Andrew Jensen. None of the Managing Members of KVA II has individual voting or investment power with respect to such shares and

each disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of KVA II is One Embarcadero, Suite 3700, San Francisco, CA 94111.

(7) Consists of 14,268 shares of common stock issuable directly to Pravin Dugel upon the conversion of options within 60 days of December 31, 2017.

(8) Consists of (i) 593,019 shares of common stock held directly by Joseph Gardner and (ii) 235,355 shares of common stock issuable upon the conversion of options within 60 days of December 31, 2017.

(9) Consists of (i) 320,536 shares of common stock held directly by Kevin G. Peters and (ii) 1,912 shares of common stock issuable upon the conversion of options within 60 days of December 31, 2017.

(10) Consists of 101,153 shares of common stock issuable directly to Steve Pakola upon the conversion of options within 60 days of December 31, 2017.

SECURITIES WE MAY OFFER

This prospectus contains summary descriptions of the securities we may offer from time to time. These summary descriptions are not meant to be complete descriptions of each security. The particular terms of any security will be described in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our amended and restated certificate of incorporation and amended and restated bylaws, which are exhibits to the registration statement of which this prospectus forms a part, and by applicable law. The terms of our common stock and preferred stock may also be affected by Delaware law.

General

Our authorized capital stock consists of 300,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of undesignated preferred stock, par value $0.0001 per share.

As of December 31, 2017, there were 27,070,038 shares of common stock outstanding and no shares of preferred stock outstanding. As of December 31, 2017, we had approximately 262 record holders of our capital stock.

Common Stock

The holders of outstanding shares of common stock are entitled to receive dividends out of assets or funds legally available for the payment of dividends of such times and in such amounts as the board from time to time may determine. Holders of common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders. There is no cumulative voting of the election of directors then standing for election. The common stock is not entitled to pre-emptive rights and is not subject to conversion or redemption. Upon liquidation, dissolution or winding up of our company, the assets legally available for distribution to stockholders are distributable ratably among the holders of the common stock after payment of liquidation preferences, if any, on any outstanding payment of other claims of creditors. Each outstanding share of common stock is duly and validly issued, fully paid and non-assessable.

Preferred Stock

Shares of preferred stock may be issued from time to time in one or more series, each of which will have such distinctive designation or title as shall be determined by our board of directors prior to the issuance of any shares thereof. Preferred stock will have such voting powers, full or limited, or no voting powers, and such preferences and relative, participating, optional or other special rights and such qualifications, limitations or restrictions thereof, as shall be stated in such resolution or resolutions providing for the issue of such class or series of preferred stock as may be adopted from time to time by the board of directors prior to the issuance of any shares thereof. Subject to the terms of any preferred stock designation that we may adopt from time to time, the number of authorized shares of preferred stock may be decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a supermajority (66 2/3%) of the voting power of all the then outstanding shares of our capital stock entitled to vote generally in the election of the directors, voting together as a single class, plus a supermajority (66 2/3%) of the voting power of the outstanding shares of each class entitled to vote thereon as a class.

While we do not currently have any plans for the issuance of additional preferred stock, the issuance of such preferred stock could adversely affect the rights of the holders of common stock and, therefore, reduce the value of the common stock. It is not possible to state the actual effect of the issuance of any shares of preferred stock on the rights of holders of the common stock until the board of directors determines the specific rights of the holders of the preferred stock; however, these effects may include:

- Restricting dividends on the common stock;

- Diluting the voting power of the common stock;
- Impairing the liquidation rights of the common stock; or
- Delaying or preventing a change in control of our company without further action by the stockholders.

Other than in connection with shares of preferred stock (as explained above), which preferred stock is not currently designated nor contemplated by us, we do not believe that any provision of our amended and restated certificate of incorporation or bylaws would delay, defer or prevent a change in control.

Warrants

In connection with the private placement offering in March 2017, we agreed to issue to Raymond James & Associates, Inc., National Securities Corporation and Katalyst Securities LLC, each a U.S. registered broker-dealer, or collectively the Placement Agents, warrants to purchase a number of shares equal to 7% of the number of shares sold in such offering, or the Placement Agent Warrants. As of the date hereof, the Placement Agent Warrants entitle their holders to purchase 317,562 shares of common stock, with a term of three years and an exercise price of $5.00 per share.

The Placement Agent Warrants contain customary provisions for adjustment in the event of stock splits, subdivision or combination, mergers, etc.

This summary descriptions of the warrants described above is qualified in their entirety by reference to the forms of such warrants filed as an exhibit to this registration statement of which this prospectus is a part.

Options

Options to purchase shares of Aerpio common stock that were originally granted under Aerpio's 2011 Plan to certain of Aerpio's employees, officers and directors were converted into option to purchase 927,592 shares of our common stock with a weighted average exercise price of $1.69 per share when they were assumed by us in connection with the Merger.

Other Convertible Securities

As of the date hereof, other than the securities described above, we do not have any outstanding convertible securities.

Registration Rights

Registration Rights Agreement. In connection with the Merger and the Offering, we entered into a Registration Rights Agreement, pursuant to which we agreed that promptly, but no later than 60 calendar days from the final closing of the Offering, we would file a registration statement with the SEC, or the Registration Statement, covering (a) the shares of common stock issued in the Offering, (b) the shares of common stock issuable upon exercise of the Placement Agent Warrants, (c) the shares of common stock issued in exchange for the equity securities of Aerpio outstanding prior to the Merger and (d) 1,000,000 shares of common stock, or collectively, the Registrable Shares. We will use our commercially reasonable efforts to ensure that such Registration Statement is declared effective within 150 calendar days after the final closing of the Offering. If we are late in filing the Registration Statement, if the Registration Statement is not declared effective within 150 days after the final closing of the Offering, if we fail to maintain the Registration Statement continuously effective as to all Registrable Shares included in such Registration Statement or the holders of Registrable Shares cannot use the Registration Statement to resell the Registrable Shares for a period of more than 15 trading days (other than suspension of the Registration Statement in connection with its post-effective amendment in connection with filing our Annual Report on Form 10-K for the time reasonably required to respond to any comments from the

SEC or during a permitted blackout period as described in the Registration Rights Agreement) or after September 15, 2017, the Registrable Shares are not listed for quotation on OTC Markets, Nasdaq, NYSE, or NYSE MKT or trading of the common stock is suspended for more than 3 consecutive trading days, we will make payments to each holder of Registrable Shares as monetary penalties at a rate equal to 12% of the Offering Price per annum for each share affected during the period; provided, however, that in no event will the aggregate of any such penalties exceed 5% of the Offering Price per share. No monetary penalties will accrue with respect to any Registrable Shares removed from the Registration Statement in response to a comment from the staff of the SEC limiting the number of shares of common stock which may be included in the Registration Statement, or Cutback Comment, or after the Registrable Shares may be resold without volume or other limitations under Rule 144 or another exemption from registration under the Securities Act. Any cutback resulting from a Cutback Comment shall be allocated first to the shares of common stock issuable upon the exercise of the Placement Agent Warrants and second to the other Registrable Shares taken together, in each case pro rata based on the total number of such shares held by or issuable to each holder in such group.

We must keep the Registration Statement effective for five years from the date it is declared effective by the SEC or until (i) the Registrable Shares have been sold in accordance with such effective Registration Statement or (ii) the Registrable Shares have been previously sold in accordance with Rule 144. We must comply with the informational requirements of Rule 144 so long as any shares of common stock issued in the Offering are subject to Rule 144, regardless of whether we are subject to filing requirements under the Exchange Act.

We will pay all expenses in connection with any registration obligation provided in the Registration Rights Agreement, including, without limitation, all registration, filing, stock exchange fees, printing expenses, all fees and expenses of complying with applicable securities laws, and the fees and disbursements of our counsel and of our independent accountants and reasonable fees and disbursements of counsel to the investors. Each investor will be responsible for its own sales commissions, if any, transfer taxes and the expenses of any attorney or other advisor such investor decides to employ.

We filed a Registration Statement on April 14, 2017 which was declared effective on June 26, 2017. Additionally, we were listed on the OTC Markets—OTCQB Tier on August 8, 2017.

Aerpio Registration Rights Agreement. In addition, we entered into a separate registration rights agreement with certain of the pre-Merger stockholders of Aerpio and their affiliates, which we refer to as the Aerpio Registration Rights Agreement. The rights granted to such stockholders under the Aerpio Registration Rights Agreement take effect following such time as the Registration Statement described above no longer remains effective. The holders of 17,544,908 shares of our common stock are entitled to rights with respect to the registration of these securities under the Securities Act. The Aerpio Registration Rights Agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Following the date on which the Aerpio Registration Rights Agreement takes effect, we will be required, upon the written request of the holders of 30% of the registrable securities under the Aerpio Registration Rights Agreement, to file a registration statement on Form S-1 (if Form S-3 is not then available to us to use) and use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the Aerpio Registration Rights Agreement. In addition, if we are eligible to file a registration statement on Form S-3, upon the written request of the holders of at least 20% of the registrable securities, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve month period pursuant to this provision of the Aerpio Registration Rights Agreement. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations. If we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the Aerpio

Registration Rights Agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering. The Aerpio Registration Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

All descriptions of the Registration Rights Agreement herein are qualified in their entirety by reference to the text thereof filed as Exhibit 10.5 hereto, and all descriptions of the Aerpio Registration Rights Agreement herein are qualified in their entirety by reference to the text thereof filed as Exhibit 10.9 hereto each of which is incorporated herein by reference.

Anti-Takeover Effects of Delaware Law and Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the price of our common stock.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits a person deemed an “interested stockholder” from engaging in a “business combination” with a publicly held Delaware corporation for three years following the date such person becomes an interested stockholder unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an “interested stockholder” is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation’s voting stock. Generally, a “business combination” includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the price of our common stock.

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of our company. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Special Stockholder Meetings

Our bylaws provide that a special meeting of stockholders may be called only by a majority of our board of directors then in office.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Classified Board; Election and Removal of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. Because our stockholders do not have cumulative voting rights, our stockholders holding a majority of the shares of our common stock outstanding will be able to elect all of our directors. In addition, our directors may not be removed without cause, and removal of our directors for cause will require a supermajority (66 2/3%) stockholder vote. For more information on the classified board of directors, see the section titled *"Management—Board Composition."* This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Choice of Forum

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, then the United States District Court for the District of Delaware) will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine.

Amendment of Charter and Bylaw Provisions

The amendment of any of the above provisions in our amended and restated certificate of incorporation and bylaws, except for the provision making it possible for our board of directors to issue convertible preferred stock, would require a supermajority (66 2/3% and majority of the minority, if applicable) stockholder vote.

Sale or Liquidation

Our amended and restated certificate of incorporation includes provisions that require the approval of a supermajority (66 2/3% and majority of the minority, if applicable) vote of the outstanding shares of our capital stock in order to consummate a liquidation event.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

Listing

Our common stock is listed on the OTC Markets—OTCQB tier under the trading symbol “ARPO.”

DESCRIPTION OF DEBT SECURITIES

This section describes the general terms and provisions of our debt securities that we may issue from time to time. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any future debt securities we may offer under this prospectus, the applicable prospectus supplement or free writing prospectus will describe the specific terms of any debt securities offered through that prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below. Unless the context requires otherwise, whenever we refer to the "indentures," we are also referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue any senior debt securities under the senior indenture that we will enter into with the trustee named in the senior indenture. We will issue any subordinated debt securities under the subordinated indenture that we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement, of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We use the term "trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement or free writing prospectus and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete applicable indenture that contains the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

- We will describe in the applicable prospectus supplement or free writing prospectus the terms of the series of debt securities being offered, including:
- the title;
- the principal amount being offered, and if a series, the total amount authorized and the total amount outstanding;
- any limit on the amount that may be issued;
- whether or not we will issue the series of debt securities in global form, and, if so, the terms and who the depository will be;
- the maturity date;
- whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;
- the annual interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place where payments will be payable;
- restrictions on transfer, sale or other assignment, if any;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, the conditions upon which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option, to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- whether the indenture will restrict our ability or the ability of our subsidiaries, if any at such time, to:
    - incur additional indebtedness;
    - issue additional securities;
    - create liens;
    - pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;
    - redeem capital stock;
    - place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;
    - make investments or other restricted payments;
    - sell or otherwise dispose of assets;
    - enter into sale-leaseback transactions;
    - engage in transactions with stockholders or affiliates;
    - issue or sell stock of our subsidiaries; or
    - effect a consolidation or merger;
- whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;
- a discussion of certain material or special United States federal income tax considerations applicable to the debt securities;
- information describing any book-entry features;
- provisions for a sinking fund purchase or other analogous fund, if any;
- the applicability of the provisions in the indenture on discharge;
- whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;

- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any additional events of default or covenants provided with respect to the debt securities, and any terms that may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus the terms on which a series of debt securities may be convertible into or exchangeable for our common stock, our preferred stock or other securities (including securities of a third-party). We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock, our preferred stock or other securities (including securities of a third-party) that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the indentures will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate. If the debt securities are convertible into or exchangeable for other securities of ours or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property must make provisions for the conversion of the debt securities into securities that the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

Unless we provide otherwise in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, the following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable at maturity, upon redemption or repurchase or otherwise, and the time for payment has not been extended;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

We will describe in each applicable prospectus supplement or free writing prospectus any additional events of default relating to the relevant series of debt securities.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal, premium, if any, and accrued interest, if any, due and

payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the unpaid principal, premium, if any, and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity or security satisfactory to it against any loss, liability or expense. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the trustee or security satisfactory to it against any loss, liability or expense or to be incurred in compliance with instituting the proceeding as trustee; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities, or other defaults that may be specified in the applicable prospectus supplement or free writing prospectus.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indentures.

Modification of Indenture; Waiver

Subject to the terms of the indenture for any series of debt securities that we may issue, we and the trustee may change an indenture without the consent of any holders with respect to the following specific matters:

- to fix any ambiguity, defect or inconsistency in the indenture;
- to comply with the provisions described above under “—Consolidation, Merger or Sale;”
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act;

- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided under "Description of Debt Securities—General," to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee;
- to provide for uncertificated debt securities and to make all appropriate changes for such purpose;
- to add to our covenants such new covenants, restrictions, conditions or provisions for the benefit of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred to us in the indenture; or
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

In addition, under the indentures, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, subject to the terms of the indenture for any series of debt securities that we may issue or as otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the stated maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption or repurchase of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that, subject to the terms of the indenture and any limitation otherwise provided in the prospectus supplement or free writing prospectus applicable to a particular series of debt securities, we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series.

At the option of the holder, subject to the terms of the indentures and the limitations applicable to global securities described in the applicable prospectus supplement or free writing prospectus, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement or free writing prospectus, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will make no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement or free writing prospectus the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series. If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs.

Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement or free writing prospectus any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of Ohio, except to the extent that the Trust Indenture Act is applicable.

Ranking of Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The subordinated indenture does not limit the amount of subordinated debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

The senior debt securities will rank equally in right of payment to all our other senior unsecured debt. The senior indenture does not limit the amount of senior debt securities that we may issue. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus and the related warrant agreements and warrant certificates. While the terms summarized below will apply generally to any warrants that we may offer, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. If we indicate in the prospectus supplement, the terms of any warrants offered under that prospectus supplement may differ from the terms described below. Specific warrant agreements will contain additional important terms and provisions and will be incorporated by reference as an exhibit to the registration statement, which includes this prospectus.

General

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities.

We will evidence each series of warrants by warrant certificates that we will issue under a separate warrant agreement. We will enter into the warrant agreement with a warrant agent. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

We will describe in the applicable prospectus supplement the terms of the series of warrants, including:

- the offering price and aggregate number of warrants offered;
- the currency for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the terms of any rights to redeem or call the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the periods during which, and places at which, the warrants are exercisable;
- the manner of exercise;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreement and warrants may be modified;
- federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

DESCRIPTION OF UNITS

We may issue units comprised of shares of common stock, shares of preferred stock, debt securities and warrants in any combination. We may issue units in such amounts and in as many distinct series as we wish. This section outlines certain provisions of the units that we may issue. If we issue units, they will be issued under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. The information described in this section may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units offered will be described in the applicable prospectus supplement. If so described in a particular supplement, the specific terms of any series of units may differ from the general description of terms presented below. We urge you to read any prospectus supplement related to any series of units we may offer, as well as the complete unit agreement and unit certificate that contain the terms of the units. If we issue units, forms of unit agreements and unit certificates relating to such units will be incorporated by reference as exhibits to the registration statement, which includes this prospectus.

Each unit that we may issue will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date. The applicable prospectus supplement may describe:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement;
- the price or prices at which such units will be issued;
- the applicable United States federal income tax considerations relating to the units;
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- any other terms of the units and of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Capital Stock,” “Description of Debt Securities” and “Description of Warrants” will apply to the securities included in each unit, to the extent relevant and as may be updated in any prospectus supplements.

Issuance in Series

We may issue units in such amounts and in as many distinct series as we wish. This section summarizes terms of the units that apply generally to all series. Most of the financial and other specific terms of a particular series of units will be described in the applicable prospectus supplement.

Unit Agreements

We will issue the units under one or more unit agreements to be entered into between us and a bank or other financial institution, as unit agent. We may add, replace or terminate unit agents from time to time. We will identify the unit agreement under which each series of units will be issued and the unit agent under that agreement in the applicable prospectus supplement.

The following provisions will generally apply to all unit agreements unless otherwise stated in the applicable prospectus supplement:

Modification without Consent

We and the applicable unit agent may amend any unit or unit agreement without the consent of any holder:

- to cure any ambiguity; any provisions of the governing unit agreement that differ from those described below;
- to correct or supplement any defective or inconsistent provision; or
- to make any other change that we believe is necessary or desirable and will not adversely affect the interests of the affected holders in any material respect.

We do not need any approval to make changes that affect only units to be issued after the changes take effect. We may also make changes that do not adversely affect a particular unit in any material respect, even if they adversely affect other units in a material respect. In those cases, we do not need to obtain the approval of the holder of the unaffected unit; we need only obtain any required approvals from the holders of the affected units.

Modification with Consent

We may not amend any particular unit or a unit agreement with respect to any particular unit unless we obtain the consent of the holder of that unit, if the amendment would:

- impair any right of the holder to exercise or enforce any right under a security included in the unit if the terms of that security require the consent of the holder to any changes that would impair the exercise or enforcement of that right; or
- reduce the percentage of outstanding units or any series or class the consent of whose holders is required to amend that series or class, or the applicable unit agreement with respect to that series or class, as described below.

Any other change to a particular unit agreement and the units issued under that agreement would require the following approval:

- If the change affects only the units of a particular series issued under that agreement, the change must be approved by the holders of a majority of the outstanding units of that series; or
- If the change affects the units of more than one series issued under that agreement, it must be approved by the holders of a majority of all outstanding units of all series affected by the change, with the units of all the affected series voting together as one class for this purpose.

These provisions regarding changes with majority approval also apply to changes affecting any securities issued under a unit agreement, as the governing document.

In each case, the required approval must be given by written consent.

Unit Agreements Will Not Be Qualified under Trust Indenture Act

No unit agreement will be qualified as an indenture, and no unit agent will be required to qualify as a trustee, under the Trust Indenture Act. Therefore, holders of units issued under unit agreements will not have the protections of the Trust Indenture Act with respect to their units.

Mergers and Similar Transactions Permitted; No Restrictive Covenants or Events of Default

The unit agreements will not restrict our ability to merge or consolidate with, or sell our assets to, another corporation or other entity or to engage in any other transactions. If at any time we merge or consolidate with, or

sell our assets substantially as an entirety to, another corporation or other entity, the successor entity will succeed to and assume our obligations under the unit agreements. We will then be relieved of any further obligation under these agreements.

The unit agreements will not include any restrictions on our ability to put liens on our assets, nor will they restrict our ability to sell our assets. The unit agreements also will not provide for any events of default or remedies upon the occurrence of any events of default.

Governing Law

The unit agreements and the units will be governed by Delaware law.

Form, Exchange and Transfer

We will issue each unit in global—i.e., book-entry—form only. Units in book-entry form will be represented by a global security registered in the name of a depositary, which will be the holder of all the units represented by the global security. Those who own beneficial interests in a unit will do so through participants in the depositary's system, and the rights of these indirect owners will be governed solely by the applicable procedures of the depositary and its participants. We will describe book-entry securities, and other terms regarding the issuance and registration of the units in the applicable prospectus supplement.

Each unit and all securities comprising the unit will be issued in the same form.

If we issue any units in registered, non-global form, the following will apply to them.

The units will be issued in the denominations stated in the applicable prospectus supplement. Holders may exchange their units for units of smaller denominations or combined into fewer units of larger denominations, as long as the total amount is not changed.

- Holders may exchange or transfer their units at the office of the unit agent. Holders may also replace lost, stolen, destroyed or mutilated units at that office. We may appoint another entity to perform these functions or perform them ourselves.
- Holders will not be required to pay a service charge to transfer or exchange their units, but they may be required to pay for any tax or other governmental charge associated with the transfer or exchange. The transfer or exchange, and any replacement, will be made only if our transfer agent is satisfied with the holder's proof of legal ownership. The transfer agent may also require an indemnity before replacing any units.
- If we have the right to redeem, accelerate or settle any units before their maturity, and we exercise our right as to less than all those units or other securities, we may block the exchange or transfer of those units during the period beginning 15 days before the day we mail the notice of exercise and ending on the day of that mailing, in order to freeze the list of holders to prepare the mailing. We may also refuse to register transfers of or exchange any unit selected for early settlement, except that we will continue to permit transfers and exchanges of the unsettled portion of any unit being partially settled. We may also block the transfer or exchange of any unit in this manner if the unit includes securities that are or may be selected for early settlement.

Only the depositary will be entitled to transfer or exchange a unit in global form, since it will be the sole holder of the unit.

Payments and Notices

In making payments and giving notices with respect to our units, we will follow the procedures as described in the applicable prospectus supplement.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods or any other method permitted by law.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the accompanying prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an "underwriter" as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over allot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offer.

FINANCIAL STATEMENTS

AERPIO PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets

	September 30, 2017 (unaudited)	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 24,828,910	$ 1,609,694
Short-term investments	50,000	50,000
Accounts receivable	39,246	4,157
Prepaid research and development contracts	323,814	353,434
Other current assets	621,807	209,038
Total current assets	25,863,777	2,226,323
Furniture and equipment, net	116,873	149,595
Deposits	20,960	20,960
Total assets	$ 26,001,610	$ 2,396,878
Liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable and accrued expenses	$ 2,586,233	$ 2,470,970
Convertible notes	—	12,386,647
Total current liabilities	2,586,233	14,857,617
Commitments and contingencies (Note 11)		
Redeemable convertible preferred stock (all classes)	—	73,757,890
Stockholders' equity (deficit):		
Common stock, $0.0001 par value per share; 300,000,000 and 17,440,436 shares authorized and 27,070,038 and 1,240,925 shares issued and outstanding at September 30, 2017 and December 31, 2016, respectively.	2,707	124
Additional paid-in capital	125,740,297	—
Accumulated deficit	(102,327,627)	(86,218,753)
Total stockholders' equity (deficit)	23,415,377	(86,218,629)
Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)	$ 26,001,610	$ 2,396,878

The accompanying notes are an integral part of these condensed consolidated financial statements.

AERPIO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations and Comprehensive Loss

	Three months ended September 30,		Nine months ended September 30,	
	2017	2016	2017	2016
Operating expenses:	*(unaudited)*		*(unaudited)*	
Research and development	$ 2,942,170	$ 3,481,261	$ 8,366,869	$ 9,374,383
General and administrative	1,814,068	1,264,054	6,732,816	3,953,808
Total operating expenses	4,756,238	4,745,315	15,099,685	13,328,191
Loss from operations	(4,756,238)	(4,745,315)	(15,099,685)	(13,328,191)
Grant income	46,824	26,561	93,720	116,185
Interest income (expense), net	59,847	(166,847)	(159,612)	(254,552)
Other income, net	—	—	—	997
Total other income (expense)	106,671	(140,286)	(65,892)	(137,370)
Net and comprehensive loss	$ (4,649,567)	$ (4,885,601)	$ (15,165,577)	$ (13,465,561)
Reconciliation of net loss attributable to common stockholders:				
Net and comprehensive loss	$ (4,649,567)	$ (4,885,601)	$ (15,165,577)	$ (13,465,561)
Extinguishment of preferred stock	—	—	—	224,224
Accretion of redeemable convertible preferred stock to redemption value	—	(1,054,657)	(943,297)	(3,098,149)
Net loss attributable to common stockholders	$ (4,649,567)	$ (5,940,258)	$ (16,108,874)	$ (16,339,486)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.17)	$ (6.69)	$ (0.81)	$ (20.01)
Weighted average number of common shares used in computing net loss per share attributable to common stockholders, basic and diluted	26,926,673	888,094	19,889,984	816,395

The accompanying notes are an integral part of these condensed consolidated financial statements.

AERPIO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders Equity (Deficit)

For the Nine Months Ended September 30, 2017

	Redeemable Convertible Preferred Stock (all classes)		Stockholders' Equity (Deficit)				
			Common Stock				
	Shares	Total	Shares	Par Value	Additional Paid-In Capital	Accumulated Deficit	Total
Balance at December 31, 2016	14,015,016	$ 73,757,890	1,240,925	$ 124	—	$ (86,218,753)	$ (86,218,629)
Adjustment of redeemable convertible preferred stock to redemption value	—	943,297	—	—	—	(943,297)	(943,297)
Conversion of redeemable convertible preferred stock	(14,015,016)	(74,701,187)	14,015,016	1,402	74,699,785	—	74,701,187
Conversion of convertible notes and accrued interest	—	—	2,744,059	274	13,447,660	—	13,447,934
Share exchange in connection with Merger	—	—	1,000,000	100	(100)	—	—
Issuance of common stock, net of issuance costs of $3,084,385	—	—	8,049,555	805	37,162,585	—	37,163,390
Issuance of common stock upon exercise of stock options	—	—	25,729	3	36,098	—	36,101
Forfeiture of restricted stock	—	—	(5,246)	(1)	1	—	—
Share-based compensation expense	—	—	—	—	394,268	—	394,268
Net and comprehensive loss	—	—	—	—	—	(15,165,577)	(15,165,577)
Balance at September 30, 2017	—	—	27,070,038	$2,707	$ 125,740,297	$ (102,327,627)	$ 23,415,377

The accompanying notes are an integral part of these condensed consolidated financial statements.

AERPIO PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows

	Nine months ended September 30,	
	2017	2016
	(unaudited)	
Operating activities:		
Net and comprehensive loss	$ (15,165,577)	$ (13,465,561)
Adjustments to reconcile net and comprehensive loss to net cash used in operating activities:		
Depreciation	39,269	53,244
Stock-based compensation	394,268	358,263
Amortization of debt issuance costs	75,561	118,554
Interest expense related to convertible note conversion	204,929	257,998
Changes in operating assets and liabilities:		
Accounts receivable	(35,089)	109,399
Prepaid expenses and current other assets	(383,149)	59,838
Accounts payable and other current liabilities	598,706	(168,018)
Net cash used in operating activities	(14,271,082)	(12,676,283)
Investing activities:		
Purchase of furniture and equipment	(6,547)	(113,297)
Net cash used in investing activities	(6,547)	(113,297)
Financing activities:		
Proceeds from exercise of stock options	36,101	18,969
Proceeds from issuances of convertible notes	297,354	9,073,062
Cash paid for debt issuance costs	—	(138,312)
Proceeds from sale of common stock	40,247,775	—
Cash paid in connection with the sale of common stock	(3,084,385)	—
Net cash provided by financing activities	37,496,845	8,953,719
Net increase (decrease) in cash and cash equivalents	23,219,216	(3,835,861)
Cash and cash equivalents at beginning of year	1,609,694	5,144,211
Cash and cash equivalents, nine months ended	$ 24,828,910	$ 1,308,350
Non-cash financing activities		
Conversion of redeemable convertible preferred stock into common stock	$ 74,701,187	$ —
Conversion of convertible notes and accrued interest into common stock	13,447,934	—
Accretion of redeemable convertible preferred stock to redemption value	943,297	3,098,149
Extinguishment of redeemable convertible preferred stock	—	(224,224)

The accompanying notes are an integral part of these condensed consolidated financial statements.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(UNAUDITED)

1. Nature of Organization and Operations

Aerpio Pharmaceuticals, Inc. (the "Company") was incorporated as Zeta Acquisition Corp. II ("Zeta") in the State of Delaware on November 16, 2007. Prior to the Merger, (as defined below), Zeta was a "shell company" (as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended).

On March 3, 2017, the Company's Board of Directors, and on March 10, 2017, the Company's pre-Merger (as defined below) stockholders, approved an amended and restated certificate of incorporation, which, among other things, increased authorized capital stock from 100,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share, to 300,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share.

On March 15, 2017, Zeta changed its name to Aerpio Pharmaceuticals, Inc. and its wholly-owned subsidiary, Aerpio Acquisition Corp., a corporation formed in the State of Delaware on March 3, 2017, merged with and into Aerpio Therapeutics, Inc., ("Aerpio"), (the "Merger"), a corporation incorporated on November 17, 2011 in the State of Delaware. Pursuant to the Merger, Aerpio remained as the surviving corporation and became the Company's wholly-owned subsidiary.

At the effective time of the Merger, the shares of the Aerpio's (i) common stock issued and outstanding immediately prior to the closing of the Merger (including restricted common stock, whether vested or unvested, issued under the Aerpio's 2011 Equity Incentive Plan), and (ii) redeemable convertible preferred stock issued and outstanding immediately prior to the closing of the Merger, were converted into shares of the Company's common stock. In addition, immediately prior to the Merger, the outstanding amounts under certain senior secured convertible notes issued by Aerpio to its pre-Merger noteholders were converted into shares of Aerpio's preferred stock, which were then converted to shares of Aerpio's common stock and subsequently were converted into shares of the Company's common stock, together with the other shares of the Aerpio's common stock described above. In addition, pursuant to the Merger Agreement options to purchase shares of the Aerpio's common stock issued and outstanding immediately prior to the closing of the Merger were assumed and converted into options to purchase shares of the Company's common stock. All the outstanding capital stock of Aerpio was converted into shares of the Company's common stock on a 2.3336572:1 basis.

As a result of the Merger, the Company acquired the business of Aerpio and will continue the existing business operations of Aerpio as a public reporting company under the name Aerpio Pharmaceuticals, Inc. Immediately after the Merger, on March 15, 2017, Aerpio converted into a Delaware limited liability company (the "Conversion").

Immediately following the Conversion, the pre-Merger stockholders of Zeta surrendered for cancellation 4,000,000 of the 5,000,000 shares of the outstanding common stock of Zeta, (the "Share Cancellation"). Following the Share Cancellation, on March 15, 2017, the Company closed a private placement offering (the "Offering") of 8,049,555 shares of the Company's common stock, at a purchase price of $5.00 per share, for net proceeds of $37.2 million and the issuance of warrants with a term of three years, to purchase 317,562 shares of the Company's common stock at an exercise price of $5.00 per share.

The Merger was treated as a recapitalization and reverse acquisition for financial reporting purposes. The Company is the legal acquirer of Aerpio in the transaction. However, Aerpio is considered the acquiring company for accounting purposes since (i) former Aerpio stockholders own in excess of 50% of the combined enterprise on a fully diluted basis immediately following the Merger and Offering, and (ii) all members of the Company's executive management and Board of Directors are from Aerpio. In accordance with "reverse merger" or "reverse acquisition" accounting treatment, the unaudited condensed consolidated interim financial statements for the period ended September 30, 2017 include the accounts of the Company and its wholly owned subsidiary, Aerpio Therapeutics, LLC. The comparative historical financial statements for periods ended prior to the date of

the Merger are the historical financial statements of Aerpio. Consequently, the assets and liabilities and the historical operations that are reflected in these condensed consolidated financial statements of the Company are those of Aerpio, which were recorded at their historical cost basis. Unless otherwise indicated, all share and per share figures reflect the exchange of each 2.3336572 shares of Aerpio capital stock, convertible notes and share based awards, then outstanding, for 1 share of the Company's common stock at the effective time of the Merger.

The Company is a biopharmaceutical company focused on advancing first-in-class treatments for ocular disease. The Company's lead product candidate, AKB-9778, a small molecule activator of the Tie2 pathway, is being developed for the treatment of diabetic retinopathy ("DR"). Tie2 signaling is essential for regulating blood vessel development and the stability of mature vessels. The Company has completed a Phase 2a clinical trial in diabetic macular edema ("DME"), a swelling of the retina that is a common cause of vision loss in patients with DR and during the second quarter of 2017, initiated a twelve month, double blind Phase 2b clinical trial in patients with DR who have not developed more serious complications such as DME or proliferative diabetic retinopathy.

In addition, the Company has two pipeline programs. AKB-4924 is a drug candidate for the treatment of inflammatory bowel disease and ARP-1536, humanized monoclonal antibody is a drug candidate for ocular disease. Humanized antibodies are antibodies from non-human species whose protein sequences have been modified to increase their similarity to antibodies produced naturally in humans. The Company completed a Phase 1a clinical trial in healthy volunteers for AKB-4924 and APR-1536 is currently in preclinical development. Further development on the pipeline programs is subject to receiving additional funding, which the Company may seek through collaborations with potential strategic and commercial partners.

The Company's operations to date have been limited to organizing and staffing the Company, business planning, raising capital, acquiring and developing its technology, identifying potential product candidates, and undertaking preclinical and clinical studies. The Company has not generated any revenues to date, nor is there any assurance of any future revenues. The Company's product candidates are subject to long development cycles, and there is no assurance the Company will be able to successfully develop, obtain regulatory approval for, or market its product candidates.

The Company is subject to a number of risks similar to other life science companies in the current stage of its life cycle, including, but not limited to, the need to obtain adequate additional funding, possible failure of preclinical testing or clinical trials, the need to obtain marketing approval for its product candidates, competitors developing new technological innovations, the need to successfully commercialize and gain market acceptance of any of the Company's products that are approved, and protection of proprietary technology. If the Company does not successfully commercialize any of its products or mitigate any of these other risks, it will be unable to generate revenue or achieve profitability.

2. Summary of Significant Accounting Policies

Basis of Presentation

The unaudited condensed consolidated financial statements have been prepared in accordance with U.S. Securities and Exchange Commission (SEC) regulations and include all of the information and disclosures required by U.S. generally accepted accounting principles ("U.S. GAAP" or "GAAP") for interim financial reporting, and, in the opinion of management include all adjustments necessary for a fair presentation of the results of operations, financial position and cash flows for each period presented. All adjustments are of a normal and recurring nature. These unaudited condensed consolidated financial statements should be read in conjunction with the consolidated financial statements of Aerpio Therapeutics Inc. for the year ended December 31, 2016, included in the Company's Registration Statement on Form S-1 filed with the SEC. The results of operations for the interim periods are not necessarily indicative of results of operations for a full year. The Company's condensed consolidated financial statements are stated in U.S. Dollars.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing proprietary therapeutics. All the assets and operations of the Company's sole operating segment are located in the U.S.

Use of Estimates

The preparation of condensed consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues, if applicable, and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls and in developing the estimates and assumptions that are used in the preparation of these condensed consolidated financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, including expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates, and whether historical trends are expected to be representative of future trends. The estimation process often may yield a range of potentially reasonable estimates of the ultimate future outcomes, and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: fair value of the Company's common stock and other equity instruments, accrued expenses, and income taxes.

Historically, the Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its common stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions, the prices at which the Company sold shares of redeemable convertible preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time, and, at December 31, 2016, a probability analysis of various liquidity events under differing scenarios, including both a potential public trading scenario and potential sale scenario. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock and other equity instruments at each valuation date.

The Company utilizes significant estimates and assumptions in determining the fair value of its common stock and other equity instruments. The Company granted stock options at exercise prices not less than the fair value of its common stock, as determined by the Board of Directors contemporaneously at the date such grants were made. The Board of Directors has historically determined the estimated fair value of the Company's common stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which the Company sold shares of common and preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time, and, for periods prior to the Offering, the likelihood of achieving a liquidity event, such as a public offering or sale of the Company.

The Company's results can also be affected by economic, political, legislative, regulatory, and legal actions. Economic conditions, such as recessionary trends, inflation, interest and monetary exchange rates, government fiscal policies, and changes in the prices of research studies, can have a significant effect on operations. While the Company maintains reserves for anticipated liabilities and carries various levels of insurance, the Company could be affected by civil, criminal, regulatory or administrative actions, claims, or proceedings.

Cash and Cash Equivalents

Cash and cash equivalents consist of all cash on hand, deposits, and funds invested in short-term investments with remaining maturities of three months or less at the time of purchase. The Company may maintain balances with its banks in excess of federally insured limits.

Short-Term Investments

Time deposits with remaining maturities of greater than three months but less than one year at the time of purchase are classified as short-term investments in the accompanying condensed consolidated balance sheets.

Grant Income

Grant income is recognized as earned based on contract work performed.

Research and Development

Costs incurred in connection with research and development activities are expensed as incurred. Research and development expense consists of (i) employee-related expenses, including salaries, benefits, travel, and stock-based compensation expense; (ii) external research and development expenses incurred under arrangements with third parties, such as contract research organizations and consultants; (iii) the cost of acquiring, developing, and manufacturing clinical study materials; (iv) facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and laboratory and other supplies; and (v) costs associated with preclinical activities and regulatory operations.

The Company enters into consulting, research, and other agreements with commercial firms, researchers, universities, and others for the provision of goods and services. Under such agreements, the Company may pay for services on a monthly, quarterly, project, or other basis. Such arrangements are generally cancellable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided to the Company by its clinical sites and vendors. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company.

Patents

Costs incurred in connection with the application for and issuances of patents are expensed as incurred.

Income Taxes

Income taxes are recorded in accordance with Financial Accounting Standards Board (“FASB”) Accounting Standards Codification (ASC) Topic 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the condensed consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities and for loss and credit carryforwards using enacted tax rates anticipated to be in effect for the year in which the differences are expected to reverse. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that some or all of the benefit will more likely than not be realized. The determination as to whether the tax benefit will more

likely than not be realized is based upon the technical merits of the tax position, as well as consideration of the available facts and circumstances. As of September 30, 2017, and December 31, 2016, the Company does not have any significant uncertain tax positions. If incurred, the Company would classify interest and penalties on uncertain tax positions as income tax expense.

Net Loss per Share Attributable to Common Stockholders

The Company's basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. The diluted net loss per share attributable to common stockholders is computed by adjusting the weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury stock method. For purposes of this calculation, redeemable convertible preferred stock, convertible notes payable, stock options to purchase common stock, warrants, and unvested restricted stock awards are considered to be common stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders as their effect is anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share attributable to common stockholders were the same for all periods presented.

For all periods presented, all share and per share amounts have been retrospectively adjusted to reflect the exchange of each 2.3336572 shares of Aerpio capital stock and share based awards then outstanding, for 1 share of the Company's common stock at the effective time of the Merger.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with FASB ASC Topic 718, *Compensation—Stock Compensation*. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock, to be recognized in the condensed consolidated statements of operations and comprehensive loss based on their fair values. All the Company's stock-based awards are subject only to service-based vesting conditions. The Company estimates the fair value of its stock-based awards using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate, and (d) expected dividends. The fair value of restricted stock awards is determined based on the Company's estimated common stock value.

Due to the lack of a public market for the trading of the Company's common stock and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company believes the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of the Company.

The Company uses the simplified method as prescribed by the SEC Staff Accounting Bulletin No. 107, *Share-Based Payment*, to calculate the expected term, as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term for options granted to employees, and utilizes the contractual term for options granted to non-employees. The expected term is applied to the stock option grant group as a whole, as the Company does not expect substantially different exercise or post-vesting termination behavior among its employee population. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options.

Compensation expense related to awards to employees is calculated on a straight-line basis by recognizing the grant date fair value over the associated service period of the award, which is generally the vesting term. Awards

to non-employees are adjusted through share-based compensation expense as the award vests to reflect the current fair value of such awards and are expensed using an accelerated attribution model.

Fair Value of Financial Instruments

The Company's financial instruments consist of cash equivalents, short-term investments, accounts receivable, and accounts payable. The Company values cash equivalents using quoted market prices. The valuation technique used to measure the fair value of short-term investments was based on observable market data. The fair value of accounts receivable and accounts payable approximate the carrying value because of their short-term nature.

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurements and Disclosures*, establishes a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available.

Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The three levels of the fair value hierarchy are described below:

- Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date
- Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly
- Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable

To the extent that a valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. There were no transfers within the fair value hierarchy in the nine months ended September 30, 2017 or September 30, 2016. The assets of the Company measured at fair value on a recurring basis as of September 30, 2017 and December 31, 2016 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
September 30, 2017				
Assets:				
Cash and cash equivalents	$24,828,910	$ —	$ —	$24,828,910
Short-term investments	—	50,000	—	50,000
Total assets	$24,828,910	$50,000	$ —	$24,878,910
December 31, 2016				
Assets:				
Cash and cash equivalents	$ 1,609,694	$ —	$ —	$ 1,609,694
Short-term investments	—	50,000	—	50,000
Total assets	$ 1,609,694	$50,000	$ —	$ 1,659,694

Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash and cash equivalents and short-term investments are the only financial instruments that potentially subject the Company to concentrations of credit risk. At September 30, 2017 and December 31, 2016, all the Company's cash was deposited in accounts at two principal financial institutions. The Company maintains its cash and cash equivalents and short-term investments with a high-quality, accredited financial institution and, accordingly, such funds are subject to minimal credit risk. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts, or other hedging arrangements.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources, if any. Comprehensive loss equaled net loss for all periods presented.

Furniture and Equipment

Furniture and equipment is stated at cost, less accumulated depreciation. Furniture and equipment is depreciated using the straight-line method over the estimated useful lives of the assets, generally three to seven years. Such costs are periodically reviewed for recoverability when impairment indicators are present. Such indicators include, among other factors, operating losses, unused capacity, market value declines, and technological obsolescence. Recorded values of asset groups of furniture and equipment that are not expected to be recovered through undiscounted future net cash flows are written down to current fair value, which generally is determined from estimated discounted future net cash flows (assets held for use) or net realizable value (assets held for sale).

Research and Development Costs

Research and development costs are expensed as incurred.

Recent Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the Company believes the impact of recently issued standards that are not yet effective will not have a material impact on its consolidated financial position or results of operations upon adoption.

In March 2016, the FASB issued ASU 2016-09, *"Improvements to Employee Share-Based Payment Accounting."* This ASU is intended to simplify accounting for share-based payments and requires that excess tax benefits for share-based payments be recorded as a reduction of income tax expense and reflected within operating cash flows rather than being recorded within equity and reflected within financing cash flows. The ASU also provides an option for companies to recognize forfeitures as they occur rather than estimating the number of awards expected to be forfeited. The Company adopted this ASU on January 1, 2017 and has applied the new guidance related to excess tax benefits on a prospective basis. The Company also elected to account for forfeitures of share-based payments as they occur. The effect of adoption was not material to the condensed consolidated financial statements.

In February 2016, the FASB issued ASU 2016-02, *Leases*. This ASU will require lessees to recognize almost all leases on the balance sheet as a right-of-use asset and a lease liability. For statement of operations purposes, the FASB retained a dual model, requiring leases to be classified as finance leases or operating leases. This update is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. The Company is currently assessing the effect that adoption of the new standard will have on its condensed consolidated financial statements.

In August 2016, the FASB issued ASU No. 2016-15, *Classification of Certain Cash Receipts and Cash Payments* (a consensus of the Emerging Issues Task Force). The amendments in ASU 2016-15 address eight specific cash flow issues and apply to all entities that are required to present a statement of cash flows under FASB Accounting Standards Codification (FASB ASC) 230, Statement of Cash Flows. The amendments in ASU 2016-15 are effective for public business entities for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted, including adoption during an interim period. The Company has not yet adopted this ASU and is currently evaluating the effect that adoption of this new standard will have on its condensed consolidated financial statements.

3. Related-Party Arrangements

Aerpio was initially capitalized in December 2011 in a spinout transaction from Akebia Therapeutics, Inc. (Akebia) to enable more rapid development of its compounds. In connection with the spinout of Aerpio from Akebia, the companies entered into shared services agreements. Under the terms of the shared services agreements, Akebia and Aerpio obtained from and provided to each other certain services, as outlined below. These agreements expired on December 31, 2016.

Below is a summary of the activities included in the statements of operations and comprehensive loss:

		Three Months Ended September 30,		Nine Months Ended September 30,	
Activity	Condensed Consolidated Financial Statement Caption	2017	2016	2017	2016
Akebia related employee costs	Research and development operating expenses	$ —	$ —	$—	$12,923
Facility-related reimbursement	Other income (expense), net	—	—	—	997

4. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses are as follows:

	September 30, 2017	December 31, 2016
Accounts payable	$ 855,423	$ 1,135,608
Professional fees	355,099	200,468
Accrued bonus	470,362	—
Accrued interest	—	483,442
Accrued vacation	103,300	52,835
Accrued project costs	749,183	541,158
Other	52,866	57,459
Total accounts payable and accrued expenses	$ 2,586,233	$ 2,470,970

5. Notes Payable to Investors

In March 2016, Aerpio entered into a senior secured convertible note financing (the “Convertible Notes” or the “Convertible Note Financing”) totaling approximately $9,000,000, with certain preferred investors of Aerpio. All preferred investors were invited to participate in the Convertible Notes Financing. At September 30, 2017 and December 31, 2016, the unamortized debt issuance costs related to Convertible Note financings was $0 and $75,561, respectively. In connection with the Convertible Note Financing, Aerpio’s Articles of Incorporation were amended such that any Aerpio preferred stockholder that did not participate in the Convertible Note Financing would have their respective shares of Aerpio preferred stock automatically converted into Aerpio common stock using a 3-to-1 conversion ratio and such preferred stockholders would lose the right to representation on the Aerpio Board of Directors and other preferred rights.

The Convertible Note Financing had two separate closings of approximately $4,500,000 each on April 14, 2016 and July 15, 2016. Certain Aerpio preferred stockholders chose not to participate in the Convertible Note Financing and their respective Aerpio preferred stock was converted into shares of Aerpio common stock in April 2016 in accordance with the terms of the Articles of Incorporation. Aerpio treated this as an extinguishment of its preferred stock. The Convertible Notes accrued interest at 8% per annum, compounded annually. The Company incurred $138,312 of costs in association with the issuance of the Convertible Notes that were amortized over the expected life of the Convertible Notes, from the date of execution through October 31, 2016. The Convertible Notes were also subject to mandatory prepayment upon the occurrence of certain events, such as a liquidation, dissolution, or the sale of Aerpio. In addition, and prior to maturity, the Convertible Notes were automatically convertible into shares of Aerpio capital stock upon the occurrence of a sale of Aerpio's capital stock in a single transaction resulting in gross proceeds to Aerpio of $30,000,000 (hereinafter referred to as an "Investor Sale"). The type and class of Aerpio capital stock of to be issued to the holder of each Convertible Note upon conversion would have been identical to the type and class of Aerpio capital stock issued in the Investor Sale. The holder of each Convertible Note was entitled to a number of shares of Aerpio capital determined by dividing (i) the outstanding principal amount of the Convertible Note plus any unpaid accrued interest by (ii) an amount equal to the price per share of Aerpio capital stock paid by the purchasers of such shares in connection with the Investor Sale. The Convertible Notes were secured by a first priority perfected security interest in all of the Aerpio's assets.

In October 2016 and February 2017, Aerpio executed an additional senior secured Convertible Note financings (the "Additional Convertible Notes" or the "Additional Convertible Note Financings") totaling approximately $3,500,000 and $300,000 respectively, with certain preferred investors of Aerpio. The terms of the Additional Convertible Notes are identical to the Convertible Notes and are treated as extensions of the original Convertible Note Financing. The Company incurred $125,935 of costs associated with these transactions, which were amortized to the maturity date of March 31, 2017. In connection with the Additional Convertible Note Financings, the Convertible Notes were amended and their respective maturity dates were extended from October 31, 2016 to March 31, 2017. The amendments are accounted for as a modification for accounting purposes.

In connection with the Merger (Note 1) the Convertible Notes and accrued interest were converted into the Company's common stock.

6. Common Stock

As of September 30, 2017 and December 31, 2016, the Company had 300,000,000 and 17,440,436 shares, respectively, of authorized common stock with par value of $0.0001 per share. On March 15, 2017, in connection with the Merger, (Note 1) all the outstanding redeemable convertible preferred stock, was converted into 14,015,016 shares of the Company's common stock and the Convertible Notes, both principal and accrued interest, were converted into 2,744,059 shares of the Company's common stock.

The common stock has the following characteristics.

Voting

The holders of common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings.

Dividends

The holders of common stock are entitled to receive dividends, if and when declared by the Board of Directors. Since the Company's inception, no dividends have been declared or paid to the holders of common stock.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution, or winding-up of the Company, the holders of common stock are entitled to share ratably in the Company's assets.

Lock-up Agreements and Other Restrictions

In connection with the Merger, each of the Company's executive officers, directors, stockholders holding substantially all of the shares of common stock issued in exchange for shares held in Aerpio immediately prior to the Merger, certain other stockholders, and certain key employees, (the "Restricted Holders"), holding at the closing date of the Merger (the "Closing Date") an aggregate of approximately 18.9 million shares of common stock, entered into lock-up agreements, (the "Lock-Up Agreements"), whereby they are restricted for a period of nine months after the Merger, or the Restricted Period, from certain sales or dispositions (including pledge) of all (or 80% in the case of the holders of 915,000 shares) of the Company's common stock held by (or issuable to) them, (such restrictions together referred to as the "Lock-Up"). The foregoing restrictions will not apply to the resale of shares of common stock by any Restricted Holder in any registered secondary offering of equity securities by the Company (and, if such offering is underwritten, with the written consent of the lead or managing underwriter), or to certain other transfers customarily excepted.

In addition, each Restricted Holder and any stockholders holding or beneficially owning 1% or more of our common stock after giving effect to the Merger, agreed, for a period of 12 months following the Closing Date, that it will not, directly or indirectly, effect or agree to effect any short sale (as defined in Rule 200 under Regulation SHO of the Securities Exchange Act of 1934 ("the Exchange Act"), whether or not against the box, establish any "put equivalent position" (as defined in Rule 16a-1(h) under the Exchange Act) with respect to the common stock, borrow or pre-borrow any shares of common stock, or grant any other right (including, without limitation, any put or call option) with respect to the common stock or with respect to any security that includes, relates to or derives any significant part of its value from the common stock or otherwise seek to hedge its position in the common stock.

Anti-dilution protection

Investors in the Offering have anti-dilution protection with respect to the shares of the Company's common stock sold in the Offering such that if within six (6) months after the initial closing of the Offering the Company issues additional shares of common stock or common stock equivalents (subject to certain exceptions), for consideration per share less than the Offering Price, or the Lower Price, each such investor will be entitled to receive from the Company additional shares of common stock in an amount such that, when added to the number of shares of common stock initially purchased by such investor and still held of record and beneficially owned by such investor at the time of the dilutive issuance, or the Held Shares, will equal the number of shares of common stock that such investor's Offering subscription amount for the Held Shares would have purchased at the Lower Price. Either (i) holders of a majority of the then-held Held Shares or (ii) a representative of the holders of the then-held Held Shares, which representative shall be appointed by three (3) investors who then hold the largest number of Held Shares, may waive the anti-dilution rights of all Offering investors with respect to a particular issuance by the Company. These anti-dilution rights were determined not to be a freestanding financial instrument and did not meet the definition of a derivative. At September 30, 2017, the anti-dilution rights were expired and the Company did not issue any additional shares of common stock or common stock equivalents during the nine-month period ended September 30, 2017.

Warrants to Purchase Common Stock

At September 30, 2017, the Company had warrants outstanding for the purchase of 317,562 shares of the Company's common stock at an exercise price of $5.00 per share. The warrants have a three-year term and expire on March 15, 2020. The Warrants were issued in connection with the Offering. At the expiration date of

the warrant, if the fair value of the Company's common stock exceeds the exercise price, the warrant will be automatically exercised and the exercise price will be fulfilled through the net share settlement provisions. The number of shares and the exercise price shall be adjusted for standard ant-dilution events such as stock splits, combinations, reorganizations, or issue shares as part of a stock dividend. Upon a change of control, the warrant holder will have the right to receive securities, cash or other properties it would have been entitled to receive had the warrant been exercised. The Warrants are equity classified instruments and do not contain contingent exercise provisions, or other features, that would preclude the Company from concluding that the Warrants are indexed solely to the Company's stock.

7. Preferred Stock

At September 30, 2017, the Company had 10,000,000 shares of preferred stock, par value $0.0001 per share, in authorized capital. No preferred stock was issued and outstanding at September 30, 2017. In connection with the Merger (Note 1), all the Aerpio redeemable convertible preferred stock issued and outstanding prior to the Merger was converted into shares of the Company's common stock.

At December 31, 2016, Aerpio's redeemable convertible preferred stock consisted of the following:

- Series A redeemable convertible preferred stock: 1,326,147 shares authorized and 1,239,338 shares issued and outstanding;
- Series A1 redeemable convertible preferred stock: 8,368,247 shares authorized and 8,289,663 shares issued and outstanding; and
- Series A2 redeemable convertible preferred stock: 4,660,573 shares authorized and 4,486,015 shares issued and outstanding.

All share and per share amounts are on an as converted basis to reflect the effect of the Merger. The rights, preferences, and privileges of the redeemable convertible preferred stock issued and outstanding prior to the Merger were as follows:

Voting

The holders of redeemable convertible preferred stock were entitled to the number of votes equal to the number of whole shares of Aerpio common stock into which the shares of redeemable convertible preferred stock were convertible. Except as provided by law or otherwise, the holders of redeemable convertible preferred stock voted together with the holders of Aerpio common stock as a single class. Certain significant actions required approval by at least 50% of the holders of redeemable convertible preferred stock voting as a single class on an as converted basis. Such significant actions include significant asset transfers, acquisitions, liquidation, amendments to the certificate of incorporation, new indebtedness, repurchase of common stock, changes in the authorized numbers of directors constituting the Board of Directors, and the declaration of dividends.

The holders of shares of redeemable convertible preferred stock were entitled to elect six members of Aerpio's Board of Directors, which was subject to reduction to not less than four directors under certain circumstances. The holders of Aerpio common stock (including any holders of all shares of redeemable convertible preferred stock on an as converted basis) were entitled to elect two members of Aerpio's Board of Directors, which was subject to reduction to one director under certain circumstances.

Dividends

Dividends were payable, if permitted by law, in accordance with redeemable convertible preferred stock terms or when and if declared by Aerpio Board of Directors. Prior to the issuance of Series A2 Preferred Stock, dividends on Series A Preferred Stock and Series A1 Preferred Stock were cumulative and accrued daily at a rate of 6% per

annum whether or not declared. As part of the Series A2 Preferred Stock issuance, the dividend provisions for Series A Preferred Stock and Series A1 Preferred Stock were retrospectively amended to be noncumulative with the cumulative provision to begin after the Series A2 Preferred Stock issuance date at a rate of 6% per annum. This amendment did not significantly affect the nature of the Series A Preferred Stock and Series A1 Preferred Stock or their fair value. Accordingly, the amendment was treated as a modification for accounting purposes.

Liquidation

In the event of any voluntary or involuntary liquidation, dissolution, or winding-up of Aerpio, or upon the occurrence of a Deemed Liquidation Event, as defined, at the election of more than 50% of the holders of Series A2 Preferred Stock and Series A1 Preferred Stock, those holders were entitled to be paid, in preference to the holders of Series A Preferred Stock and Aerpio common stock, out of the assets of Aerpio available for distribution at $4.90 per share for Series A2 Preferred Stock and $3.97 per share for Series A1 Preferred Stock, plus any accrued but unpaid dividends. After the holders of Series A1 Preferred Stock and Series A2 Preferred Stock are satisfied, the holders of Series A Preferred Stock were paid at $4.27 per share, plus any accrued but unpaid dividends before any payment was made to the holders of Aerpio's common stock.

In the event the assets of Aerpio available for distribution to stockholders were insufficient to pay the full amount to which the holder was entitled, the holders of Series A2 Preferred Stock and Series A1 Preferred Stock would share ratably any assets available for distribution in proportion to their relative original investment amounts. Any remaining assets of Aerpio would be distributed ratably among the holders of Series A Preferred Stock based upon aggregate applicable dividends accrued on Series A Preferred Stock not previously paid.

After the payment of all preferential amounts required to be paid to the holders of redeemable convertible preferred stock, the remaining assets available for distribution would be distributed among the holders of redeemable convertible preferred stock and Aerpio common stock based on the pro rata number of shares held by each holder, treating such securities as if they had been converted to Aerpio common stock immediately prior to such dissolution, liquidation, or winding-up of Aerpio.

Conversion

Each share of redeemable convertible preferred stock was convertible at the option of the holder, at any time and from time to time, into fully paid and non-assessable shares of Aerpio common stock. The initial conversion ratio was one share of redeemable convertible preferred stock for one share of Aerpio's common stock. The applicable conversion rate was subject to adjustments upon the occurrence of certain events.

Each share of redeemable convertible preferred stock was automatically convertible into fully paid and non-assessable shares of Aerpio common stock at the then-applicable conversion ratio, as defined, upon either: (i) the closing of the sale of shares of Aerpio's common stock to the public in an underwritten public offering at a price of $14.70 resulting in at least $40,000,000 of gross proceeds, or (ii) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of more than 50% of the then outstanding shares of redeemable convertible preferred stock on an as-converted basis.

Aerpio evaluated each series of its redeemable convertible preferred stock and determined that each individual series is considered an equity host under ASC Topic 815, Derivatives and Hedging. In making this determination, Aerpio's analysis followed the whole instrument approach, which compares an individual feature against the entire redeemable convertible preferred stock instrument that includes that feature. Aerpio's analysis was based on a consideration of the economic characteristics and risks of each series of redeemable convertible preferred stock. More specifically, Aerpio evaluated all the stated and implied substantive terms and features, including: (i) whether the redeemable convertible preferred stock included redemption features, (ii) how and when any redemption features could be exercised, (iii) whether the holders of redeemable convertible preferred stock were entitled to dividends, (iv) the voting rights of the redeemable convertible preferred stock, and (v) the existence

and nature of any conversion rights. Aerpio concluded that as the redeemable convertible preferred stock represents an equity host, the conversion feature included in all series of redeemable convertible preferred stock is clearly and closely related to the associated host instrument. Accordingly, the conversion feature of all series of redeemable convertible preferred stock was not considered an embedded derivative that required bifurcation.

Aerpio accounted for potentially beneficial conversion features under ASC Topic 470-20, Debt with Conversion and Other Options. At the time of each of the issuances of redeemable convertible preferred stock, Aerpio's common stock into which each series of the redeemable convertible preferred stock was convertible had an estimated fair value less than the effective conversion prices of the redeemable convertible preferred stock. Therefore, there was no beneficial conversion element on the respective commitment dates.

In March 2016, in connection with the Convertible Note Financing described more fully in Note 5, Aerpio's Articles of Incorporation were amended such that any preferred stockholder that did not participate in the Convertible Note Financing would have their respective shares of redeemable convertible preferred stock automatically converted into Aerpio common stock using a 3-to-1 conversion ratio and such preferred stockholders would lose the right to representation on Aerpio's Board of Directors and other preferred rights. The amendment did not represent an increase in value to the preferred stockholders and was treated as a modification to the redeemable convertible preferred stock for accounting purposes. Certain shares of redeemable convertible preferred stock held by preferred stockholders that elected to not participate in the Convertible Note Financing were converted to shares in Aerpio's common stock.

Redemption

The redeemable convertible preferred stock was redeemable on or after July 31, 2017, upon a request by more than 50% of the holders of redeemable convertible preferred stock then outstanding, payable in three annual installments commencing not more than 60 days following receipt by notice at a price equal to the greater of (i) the applicable original purchase price and dividends accrued but unpaid (Applicable Accrued Value), which is equal to its liquidation preference, or (ii) the redeemable convertible preferred stock fair value per share. Due to this redemption option, the redeemable convertible preferred stock was recorded in the mezzanine equity and subject to subsequent measurement under the guidance provided under ASC 480-10-S99. In accordance with that guidance, Aerpio elected to recognize changes in redemption value immediately as they occur through adjustments to the carrying amounts of the instruments at the end of each reporting period. As of December 31, 2016, the redemption values of all series of redeemable convertible preferred stock were equal to their respective Applicable Accrued Value. The fair values of redeemable convertible preferred stock were based upon a hybrid of the probability-weighted expected returns method and an option pricing model (OPM), which is a nonrecurring Level 3 fair value measurement within the fair value hierarchy. Under this hybrid model, share value is based on the probability weighted value of Aerpio in a potential public trading scenario, in which the redeemable convertible preferred stock converted to Aerpio common stock, and a second scenario in which equity value is allocated using the OPM. For the public trading scenario, Aerpio used the guideline public company method under the market approach.

8. Stock-Based Compensation

Pursuant to the Merger (Note 1), the Company assumed each option to purchase Aerpio common stock that remained outstanding under the Aerpio Therapeutics, Inc. 2011 Equity Incentive Plan (the "2011 Plan"), whether vested or unvested, and converted it into an option to purchase such number of shares of the Company's common stock equal to the number of shares of Aerpio common stock subject to the option immediately prior to the Merger, divided by the applicable Merger exchange rate of 2.3336572, with any fraction rounded down to the nearest whole number. The exercise price per share of each assumed option is equal to the exercise price of the Aerpio option prior to the assumption, multiplied by the applicable Merger exchange rate of 2.3336572, rounded up to the nearest whole cent. The terms of the 2011 Plan continue to govern the options covering an aggregate of 898,962 and 927,592 shares of the Company's common stock at September 30, 2017 and December 31, 2016

respectively, subject to awards assumed by the Company, except that all references in the 2011 Plan to Aerpio, will now be the Company. In addition, each unvested share of Aerpio restricted common stock issued under the 2011 Plan that was outstanding immediately prior to the effective time of the Merger, was converted by virtue of the Merger into restricted common stock of the Company, equal to the number of shares of Aerpio common stock subject to the unvested shares of Aerpio restricted common stock immediately prior to the Merger divided by the applicable Merger exchange rate of 2.3336572, with any fraction rounded down to the nearest whole number.

In March 2017, the Company's Board of Directors adopted, and the stockholders approved, the 2017 Stock Option and Incentive Plan (the "2017 Plan"), that became effective in April 2017. The 2017 Plan provides for the issuance of incentive awards up to 4,600,000 shares of common stock to officers, employees, consultants and directors, less the number of shares subject to issued and outstanding awards under the 2011 Plan that were assumed in the Merger. The 2017 Plan also provides that the number of shares reserved for issuance thereunder will be increased annually on the first day of each year beginning in 2018 by four percent (4%) of the shares of our common stock outstanding on the last day of the immediately preceding year or such smaller increase as determined by our Board of Directors. No awards were granted under the 2017 Plan as of September 30, 2017.

Stock Options

The options granted generally vest over 48 months. For employees with less than one year's service, options vest in installments of 25% at the one-year anniversary and thereafter in 36 equal monthly installments beginning in the 13th month after the initial Vesting Commencement Date (as defined), subject to the employee's continuous service with the Company. Options granted to other employees vest in 48 equal monthly installments after the initial Vesting Commencement Date, subject to the employee's continuous service with the Company. The options generally expire ten years after the date of grant. The fair value of the options at the date of grant is recognized as an expense over the requisite service period. No option awards were granted in the nine months ended September 30, 2017 and one option award was granted for 50,228 shares in the nine months ended September 30, 2016.

The following table summarizes the stock option activity during the nine-months ended September 30, 2017:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding, January 1, 2017	927,592	$ 1.70	7.48	$1,030,217
Granted	—	—		
Exercised	(25,729)	1.40		
Expired/cancelled	(2,901)	2.11		
Outstanding, September 30, 2017	898,962	$ 1.70	6.61	$3,862,412
Expected to vest, September 30, 2017	188,925	$ 1.78	7.77	$ 797,234
Options exercisable, September 30, 2017	710,037	$ 1.68	6.30	$3,065,178

Aggregate intrinsic value represents the estimated fair value of the Company's common stock at the end of the period in excess of the weighted average exercise price multiplied by the number of options outstanding or exercisable.

Compensation expense for stock options was $53,814 and $39,100 for the three months ended September 30, 2017 and 2016, respectively and $173,888 and $124,141 for the nine months ended September 30, 2017 and 2016 respectively. As of September 30, 2017, there was $201,221 of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted average period of 2.0 years.

Restricted Stock

Shares of restricted stock generally have similar vesting terms as stock options. A summary of the Company's restricted stock activity and related information during the nine months ended September 30, 2017 is as follows:

	Shares	Weighted Average Grant Date Fair Value
Nonvested, January 1, 2017	241,096	$ 1.91
Granted	—	—
Vested	(106,015)	1.77
Forfeited	(5,246)	2.20
Nonvested, September 30, 2017	129,835	$ 1.99

The Company recognized compensation expense for restricted stock of $73,545 and $74,398 for the three months ended September 30, 2017 and 2016, respectively, and $220,380 and 234,122 for the nine months ended September 30, 2017 and 2016 respectively. As of September 30, 2017, there was $248,517 of unrecognized compensation cost related to these restricted stock grants, which is expected to be recognized over a weighted average period of 1.2 years.

Compensation Expense Summary

The Company has recognized the following compensation cost related to employee and non-employee stock-based compensation activity:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Research and development	$ 88,443	$ 71,752	$276,778	$228,429
General and administrative	38,916	41,746	117,490	129,834
Total	$127,359	$113,498	$394,268	$358,263

The Company uses the Black-Scholes option pricing model to determine the estimated fair value for stock-based awards. There were no options granted in the nine months ended September 30,2017. Option pricing models require the input of various subjective assumptions, including the option's expected life, expected dividend yield, price volatility and risk-free interest rate of the underlying stock. Accordingly, the weighted-average fair value of the options granted during the three and nine months ended September 30, 2016 was $1.22. The calculation was based on the following assumptions.

	Three Months Ended September 30, 2016	Nine Months Ended September 30, 2016
Expected term (years)	n/a	6.00
Risk-free interest rate	n/a	1.39%
Expected volatility	n/a	78.00%
Expected dividend yield	n/a	0.00%

9. Income Taxes

The Company did not record a current or deferred income tax expense or benefit for the nine months ended September 30, 2017 and 2016, due to the Company's net losses and increases in its deferred tax asset valuation allowance.

10. Net Loss per Share Attributable to Common Stockholders

The following table sets forth the computation of the Company's basic and diluted net loss per share attributable to common stockholders for the periods presented:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Net and comprehensive loss	$ (4,649,567)	$ (4,885,601)	$ (15,165,577)	$ (13,465,561)
Extinguishment of preferred stock	—	—	—	224,224
Accretion of redeemable convertible preferred stock to redemption value	—	(1,054,657)	(943,297)	(3,098,149)
Net loss attributable to common stockholders	$ (4,649,567)	$ (5,940,258)	$ (16,108,874)	$ (16,339,486)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.17)	$ (6.69)	$ (0.81)	$ (20.01)
Weighted average common shares used in computing net loss per share attributable to common stockholders, basic and diluted	26,926,673	888,094	19,889,984	816,395

The following weighted average common stock equivalents were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods presented because including them would have had an anti-dilutive effect:

	Three and Nine Months Ended September 30,	
	2017	2016
Convertible preferred stock (if converted)	—	14,141,112
Notes and accrued interest (if converted)	—	1,904,034
Options to purchase common stock	898,962	927,592
Unvested restricted stock	129,835	292,183
Warrants to purchase common stock	317,562	—

11. Commitments and Contingencies

The Company is a party to a lease covering 7,580 square feet of space in Cincinnati, Ohio that expires in June 2018. Total rent expense for all operating leases was $53,071 and $54,320 for the three months ended September 30, 2017 and 2016, respectively and $155,513 and $162,424 the nine months ended September 30, 2017 and 2016, respectively. The lease agreement contains free rent, escalating rent payments and reimbursement for tenant improvements that amounted to $0 and $46,390 in the three and nine months ended September 30, 2016, respectively. No such lease incentives were recognized in 2017. Rent expense is recorded on the straight-line basis over the initial term with the differences between rent expense and rent payments recorded as deferred rent. As of September 30, 2017, the Company had deferred rent of $44,566, which is included in accrued expenses in the accompanying condensed consolidated balance sheet. As of September 30, 2017, non-cancelable future minimum lease payments under the existing operating lease were $79,357. As of September 30, 2017, future payments related to operating leases activities are presented in the table below.

	2017	2018	2019 and Thereafter	Total
Operating leases	$26,379	$52,978	$ —	$79,357

The Company contracts with various organizations to conduct research and development activities, including clinical trial organizations to manage clinical trial activities. The scope of the services under these research and development contracts can be modified and the contracts cancelled by the Company upon written notice. In the event of a cancellation, the Company would only be liable for the cost and expenses incurred to date.

12. Employee Stock Purchase Plan

In March 2017, the Board of Directors adopted and the stockholders approved, the Employee Stock Purchase Plan (the “ESPP”), that became effective in April 2017. The ESPP provides for the issuance of up to 300,000 shares of the Company’s common stock for the purchases made under the ESPP. The ESPP also provides that the number of shares reserved for issuance thereunder will be increased annually on the first day of each year beginning in 2018 by one percent (1%) of the shares of the Company’s common stock outstanding on the last day of the immediately preceding year or such smaller increase as determined by the Company’s Board of Directors. The Board of Directors has not yet determined the timing for the offering periods under the ESPP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited the financial statements of Aerpio Pharmaceuticals, Inc. at December 31, 2016 and 2015, and for each of the two years in the period ended December 31, 2016, as set forth in their report dated March 9, 2017 (except for the paragraphs included under the caption “Merger and Offering” described in Notes 1 and 15, as to which the date is May 22, 2017), included in the Aerpio Pharmaceuticals, Inc. Registration Statement (Form S-1 No. 333-217320) and incorporated by reference herein. The financial statements of Aerpio Pharmaceuticals, Inc. are incorporated by reference in reliance on Ernst & Young LLP’s report, given on their authority as experts in accounting and auditing.

LWBJ, LLP, independent registered accounting firm, has audited the financial statements of Zeta Acquisition Corp. II at December 31, 2015 and 2016, and for the years then ended, as set forth in their report dated March 7, 2017, included in the Aerpio Pharmaceuticals, Inc. Registration Statement (Form S-1 No. 333-217320) and incorporated by reference herein. The financial statements of Zeta Acquisition Corp. II are incorporated by reference in reliance on LWBJ, LLP’s report, given on their authority as experts in accounting and auditing.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Any underwriters will also be advised about the validity of the securities and other legal matters by their own counsel, which will be named in the prospectus supplement.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. For further information, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Statements contained in this prospectus or incorporated by reference concerning the contents of any contract or any other document are not necessarily complete. If a contract or document has been filed or incorporated by reference as an exhibit to the registration statement, we refer you to the copy of the contract or document that has been filed. Each statement in this prospectus or incorporated by reference relating to a contract or document filed as an exhibit is qualified in all respects by the filed exhibit. The reports and other information we file with the SEC can be read and copied at the SEC's Public Reference Room at 100F Street, NE, Washington D.C. 20549. Copies of these materials can be obtained at prescribed rates from the Public Reference Section of the SEC at the principal offices of the SEC, 100 F Street, NE, Washington D.C. 20549. You may obtain information regarding the operation of the public reference room by calling 1(800) SEC-0330. The SEC also maintains a web site *(http://www.sec.gov)* that contains reports, proxy and information statements and other information regarding issuers like us that file electronically with the SEC.

We are subject to the reporting and information requirements of the Exchange Act and, as a result, we file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the SEC's public reference room and the web site of the SEC referred to above.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made after the date of the filing of this registration statement and prior to the effectiveness of this registration statement, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus and prior to the termination of this offering:

- Annual Report on Form 10-K for the year ended December 31, 2016;
- Quarterly Reports on Form 10-Q filed with the SEC for the quarters ended March 31, 2017, June 30, 2017 and September 30, 2017;
- Current Reports on Form 8-K filed with the SEC on March 13, 2017, March 17, 2017, June 29, 2017, July 31, 2017, August 8, 2017, October 10, 2017, November 14, 2017, and December 18, 2017; and
- Registration Statement on Form S-1 filed with the SEC on April 14, 2017, and declared effective on June 23, 2017.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus, including exhibits to these documents. You should direct any requests for documents to Investor Relations, Aerpio Pharmaceuticals, Inc., 9987 Carver Road, Cincinnati, OH 45242; telephone: (513) 985-1920.

You also may access these filings on our website at www.aerpio.com. We do not incorporate the information on our website into this prospectus or any supplement to this prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus or any supplement to this prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus or any supplement to this prospectus).

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed modified, superseded or replaced for purposes of this prospectus to the extent that a statement contained in this prospectus modifies, supersedes or replaces such statement.

$150,000,000

Common Stock
Preferred Stock
Debt Securities
Warrants
Units

PROSPECTUS

, 2018

We have not authorized any dealer, salesperson or other person to give any information or represent anything not contained in this prospectus. You must not rely on any unauthorized information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus does not offer to sell any securities in any jurisdiction where it is unlawful. Neither the delivery of this prospectus, nor any sale made hereunder, shall create any implication that the information in this prospectus is correct after the date hereof.

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The information contained in this prospectus supplement is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus supplement is not an offer to sell these securities and is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated February 21, 2018

PROSPECTUS SUPPLEMENT

aerpio

Up to $75,000,000

Common Stock

We have entered into a Controlled Equity Offering℠ Sales Agreement, or the sales agreement, with Cantor Fitzgerald & Co., or Cantor, pursuant to which we may offer and sell our common stock from time to time through Cantor, acting as agent, having an aggregate offering price of up to $75,000,000.

Sales of our common stock, if any, under this prospectus supplement may be made in sales deemed to be "at the market offerings" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. Cantor will act as sales agent on a best efforts basis and use commercially reasonable efforts to sell on our behalf all of the common stock requested to be sold by us, consistent with its normal trading and sales practices, on mutually agreed terms between Cantor and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Cantor will be entitled to compensation under the terms of the sales agreement at a commission rate of up to 3.0% of the gross sales price per share sold. In connection with the sale of common stock on our behalf, Cantor will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Cantor will be deemed to be underwriting commissions or discounts.

Our common stock is listed on the OTC Markets—OTCQB Tier under the symbol "ARPO." On February 16, 2018, the last reported sale price of our common stock on the OTCQB was $4.50 per share.

Investing in our common stock involves risks. Before making an investment decision, you should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page S-7 and under similar headings in the other documents that are incorporated by reference herein.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or the accuracy of this prospectus supplement. Any representation to the contrary is a criminal offense.

CANTOR Fitzgerald

The date of this prospectus supplement is , 2018.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement, together with the information incorporated by reference as described under the headings "Where You Can Find More Information" and "Documents Incorporated by Reference" in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

This prospectus supplement describes the specific terms of the common stock we are offering and also adds to, and updates information contained in the documents incorporated by reference into this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference into this prospectus supplement that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference into this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in, or incorporated by reference into, this prospectus supplement and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and Cantor has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and Cantor is not, making an offer to sell or soliciting an offer to buy our common stock in any jurisdiction in which an offer or solicitation is not authorized or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should assume that the information appearing in this prospectus supplement, the documents incorporated by reference into this prospectus supplement, and in any free writing prospectus that we may authorize for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the documents incorporated by reference into this prospectus supplement, and any free writing prospectus that we may authorize for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Documents Incorporated by Reference."

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and any applicable prospectus supplement or free writing prospectus, including the documents that we incorporate by reference herein, includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the "Securities Act," and Section 21E of the Securities Exchange Act of 1934, as amended, or the "Exchange Act." For this purpose, any statements contained herein, other than statements of historical fact, including statements regarding the progress and timing of our product development programs and related trials; our future opportunities; our strategy, future operations, anticipated financial position, future revenues and projected costs; our management's prospects, plans and objectives; and any other statements about management's future expectations, beliefs, goals, plans or prospects constitute forward-looking statements. We may, in some cases, use words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "project," "should," "target," "will," "would" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the risks described under the heading "Risk Factors" in this prospectus supplement and the risk factors and cautionary statements described in other documents that we file from time to time with the SEC, specifically under "Item 1A. Risk Factors" and elsewhere in our Quarterly Reports on Form 10-Q for the quarters ended September 30, 2017, June 30, 2017 and March 31, 2017, and our Current Reports on Form 8-K. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any acquisitions, mergers, dispositions, business development transactions, joint ventures or investments we may enter into or make in the future.

You should rely only on information contained, or incorporated by reference, in this prospectus supplement, the registration statement of which this prospectus supplement is a part, the documents incorporated by reference in this prospectus supplement, and any applicable prospectus supplement or free writing prospectus and understand that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law. Before deciding to purchase our securities, you should carefully consider the risk factors included or incorporated herein by reference, in addition to the other information set forth in this prospectus supplement, any accompanying prospectus supplement, any free writing prospectus and in the documents incorporated by reference.

OUR COMPANY

This business overview highlights information contained in certain documents incorporated by reference into this prospectus supplement. This business overview does not contain all of the information that you should consider before investing in our common stock. You should read the entire prospectus carefully, including the "Risk Factors" section and the financial statements and the notes to those statements incorporated herein by reference, before making an investment decision.

References in this prospectus supplement to the terms "Aerpio Pharmaceuticals," "company," "we," "our" or "us" or other similar terms means Aerpio Pharmaceuticals, Inc.

Overview

Aerpio is a biopharmaceutical company focused on advancing first-in-class treatments for ocular disease. Our lead product candidate, AKB-9778, a small molecule activator of the Tie2 pathway, is being developed for the treatment of diabetic retinopathy, or DR, a disease characterized by progressive compromise of blood vessels in the back of the eye. The Tie2 receptor is expressed almost exclusively in endothelial cells (cells that make up blood vessels) and is essential for regulating vascular stability and preventing blood vessel compromise associated with diabetes. We have completed a Phase 2a trial of AKB-9778 in 144 patients with diabetic eye disease. Based on the results from this trial, we believe AKB-9778 has the potential to reverse the damage to blood vessels caused by diabetes. In contrast to marketed treatments for DR that are administered by a physician via intraocular injection, we intend to deliver AKB-9778 systemically by self-administered subcutaneous injection, similar to insulin. We believe that this delivery method provides an opportunity to treat diabetic eye disease at an earlier stage and reduces the likelihood of developing vision-threatening complications. In June 2017, we initiated a 48-week, double-masked, Phase 2b clinical trial, which we refer to as TIME-2b, in patients with DR who have not developed more serious complications such as diabetic macular edema, or DME or proliferative diabetic retinopathy, or PDR.

According to the World Health Organization's Global Report of Diabetes, there are an estimated 422 million individuals living with diabetes worldwide. An estimated 34.6% of these individuals, or 146 million people, have DR, 6.81%, or 28 million, have DME and 6.96%, or 29.7 million, have PDR. The underlying problem in diabetic complications is damage to the blood vessels, commonly referred to as diabetic vasculopathy, which is caused by chronic hyperglycemia. This damage causes blood vessels to leak fluid and proteins into the surrounding tissue, leading to complications. In the eyes, this damage leads to DR which can progress to DME and/or PDR. In other parts of the body such as the kidney, the damage leads to diabetic nephropathy and in the lower extremities, the damage leads to non-healing foot ulcers, peripheral artery disease and critical limb ischemia. These diabetic complications lead to life- and sight-threatening conditions including kidney dialysis, amputations and blindness that are costly to treat. Diabetic patients with complications are estimated to cost the health care system 3.5 times more than patients without complications. For example, dialysis patients cost an average of $89,000 per year and the cost for the first year of DME therapy with Eylea® is $14,400 per eye based on published Medicare allowable charges per dose and the frequency of dosing as approved by the FDA. If approved, we believe that systemic treatment with AKB-9778 could have the potential to change the treatment paradigm for diabetics in the future and potentially address a major societal problem by lowering the cost of care associated generally with diabetes.

Diabetic eye disease is one of the most common and debilitating complications of diabetes. Over time, diabetes damages blood vessels in the back of the eye. When this happens, a patient is said to have DR. Eventually, these damaged blood vessels can leak blood proteins and fluid into the central portion of the retina, called the macula, which is responsible for high resolution central vision. The leakage of protein and fluid into the macula causes swelling, a condition called DME. The more progressive stages of DR, referred to as PDR, are characterized by the growth of abnormal new blood vessels. These new blood vessels can bleed into the eye and if left untreated can result in decreased visual acuity and eventual blindness. The likelihood of a person developing these sight-threatening complications increases as DR progresses.

According to the 2017 revenue reports for Regeneron and Roche, sales of the two leading approved therapies for DME, Eylea (aflibercept), which is marketed by Regeneron and Lucentis (ranibizumab), which is marketed by Genentech and Novartis, were estimated to be over $5.6 billion worldwide in 2017. Given that the number of patients with DR is roughly five times that for DME, we believe that a therapy that can reverse early ocular damage in patients with DR and slow or prevent the development of DME or PDR, without requiring repeated injections into the eye, could have substantial clinical and commercial value.

AKB-9778 is a small molecule activator of the Tie2 pathway that we believe helps to stabilize blood vessel walls and prevent vascular compromise in the eye, and based on pre-clinical models, potentially elsewhere in the body. Such vascular compromise in the eye may eventually lead to DME or PDR and, in many cases, to loss of vision or even blindness. We believe AKB-9778's mechanism of action reduces vascular damage and restores vascular integrity. In contrast to current therapies for diabetic eye disease, which are all administered by a physician via repeated injections into the eye, AKB-9778 is being developed as a self-administered subcutaneous injection that allows for treatment of both eyes.

In addition to DR, the Tie2 pathway is also implicated in other diabetic complications. We believe systemic treatment with AKB-9778 may address diabetic nephropathy and peripheral vascular disease. If we are successful in developing and commercializing AKB-9778 for DR, we intend to conduct longer term clinical trials to evaluate AKB-9778's potential to reduce or delay the need for kidney dialysis and reduce amputations.

The TIME-2b study is a double-masked, placebo-controlled multi-center trial that is currently ongoing and has enrolled 167 patients randomized evenly to receive either AKB-9778 15 mg subcutaneously once daily, AKB-9778 15 mg subcutaneously twice daily or placebo for a 48-week treatment period. The primary endpoint of the TIME-2b study is the percentage of patients who improve by 2 or more steps in DR Severity Score, or DRSS, in the study eye.

There is emerging scientific literature that supports the role of Tie 2 in the maintenance of conventional outflow, or CO, pathway in the front of the eye. Existing preclinical and clinical evidence suggest the potential of AKB-9778 for reducing intraocular pressure in primary open angle glaucoma, or POAG, and ocular hypertension. We plan to initiate a Phase 1b clinical trial in the first quarter of 2019 to evaluate AKB-9778 for POAG and, if we observe positive results, we expect to initiate a Phase 2 program for this indication.

We are also developing AKB-4924, a selective stabilizer of hypoxia-inducible factor-1 alpha, or HIF-1 alpha, that is being developed for the treatment of inflammatory bowel disease. HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. We have completed a single ascending dose clinical trial in healthy volunteers for AKB-4924 and plan to initiate a multiple ascending dose, or MAD study in the second quarter of 2018. If we successfully complete the MAD study, we expect to initiate a Phase 1b clinical study of AKB-4924 in patients with ulcerative colitis in the second half of 2018.

ARP-1536, our humanized monoclonal antibody directed at the same target as AKB-9778, is in preclinical development. We are evaluating development options for ARP-1536, including once-monthly subcutaneous injection for the treatment of diabetic vascular complications and once-monthly intravitreal injection for the treatment of advanced diabetic eye disease such as DME or PDR.

Company Information

We were originally incorporated in the State of Delaware in November 2007 under the name "Zeta Acquisition Corp. II." Prior to the Merger, Zeta Acquisition Corp. II was a "shell" company registered under the Exchange Act with no specific business plan or purpose until it began operating the business of Aerpio through the Merger transaction on March 15, 2017. Aerpio was incorporated in the State of Delaware in November 2011 to focus primarily on advancing first-in-class treatments for ocular disease. Effective upon the Merger, a wholly-owned subsidiary of Zeta Acquisition Corp. II merged with and into Aerpio, and Aerpio continued as the operating

subsidiary of Zeta Acquisition Corp. II. Immediately following the Merger, Aerpio converted into a Delaware limited liability company with the name Aerpio Therapeutics LLC.

Our corporate headquarters are located at 9987 Carver Road, Cincinnati, Ohio 45242, and our telephone number is (513) 985-1920. We maintain a website at www.aerpio.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission, or SEC, will be available free of charge through the website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this prospectus supplement or our other filings with the SEC.

All brand names or trademarks appearing in this prospectus supplement are the property of their respective holders. Use or display by us of other parties' trademarks, trade dress, or products in this prospectus supplement is not intended to, and does not, imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owners.

THE OFFERING

Common stock offered by us	Common stock having an aggregate offering price of up to $75,000,000.
Common stock to be outstanding after this offering	43,736,704 common stock
Plan of Distribution	“At the market offering” that may be made from time to time through our agent, Cantor. See “Plan of Distribution.”
Use of Proceeds	We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, but are not limited to, working capital, strategic acquisitions and other potential business development activities, ongoing research and development activities and capital expenditures. See “Use of Proceeds”.
Risk Factors	Investing in our common stock involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading “Risk Factors” in this prospectus supplement and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement, together with the other information included in or incorporated by reference into this prospectus supplement, before deciding whether to invest in our common stock.
OTCQB symbol	ARPO

The number of common stock to be outstanding after this offering and, unless otherwise indicated, the information in this prospectus supplement are based on 27,070,038 shares of common stock outstanding as of December 31, 2017 and assumes the sale and issuance of $75,000,000 of common stock at $4.50 per share, the last reported sale price of our common stock on the OTCQB on February 16, 2018, and excludes 4,571,370 shares of common stock held by us for issuance under our equity incentive plans as of December 31, 2017, of which there were outstanding options to purchase 1,179,410 shares of common stock at a weighted average exercise price of $2.61 per share, and excludes an additional 280,448 shares of common stock outside of our equity incentive plans issuable upon the exercise of options at a weighted average exercise price of $5.50 per share.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described below and incorporated herein by reference, including (i) our quarterly reports on Form 10-Q for the quarter ended September 30, 2017, June 30, 2017 and March 31, 2017, each of which is incorporated by reference into this prospectus supplement and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus supplement, as updated or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement, together with the other information in this prospectus supplement, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also carefully read the section below entitled "Cautionary Note Regarding Forward-Looking Statements."

Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering, and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Accordingly, you will be relying on the judgment of our management with regard to the use of any proceeds from the sale of common stock in this offering, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 16,666,666 of our common stock are sold at a price of $4.50 per share pursuant to this prospectus supplement, which was the last reported sale price of our common stock on the OTCQB on February 16, 2018, for aggregate gross proceeds of $75,000,000, after deducting commissions and estimated aggregate offering expenses payable by us, you would experience immediate dilution of $2.30 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2017, after giving effect to this offering and the assumed offering price. The exercise of outstanding share options may result in further dilution of your investment. See the section entitled "Dilution" below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing shareholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

USE OF PROCEEDS

We intend to use the net proceeds from this offering, if any, for general corporate purposes, which may include, but are not limited to, working capital, strategic acquisitions and other potential business development activities, ongoing research and development activities and capital expenditures. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the timing and application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short-term, interest-bearing instruments.

DILUTION

If you invest in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share and the as adjusted net tangible book value per share after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is tangible assets less total liabilities, by the number of our outstanding common stock. Dilution represents the difference between the portion of the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of September 30, 2017, was $23,415,377, or $0.86 per share.

After giving effect to the sale of our common stock pursuant to this prospectus supplement in the aggregate amount of $75,000,000 at an assumed offering price of $4.50 per share, the last reported sale price of our common stock on the OTCQB on February 16, 2018, and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of September 30, 2017 would have been $96,335,377, or $2.20 per common stock. This represents an immediate increase in the net tangible book value of $1.34 per share to our existing shareholders and an immediate dilution in net tangible book value of $2.30 per share to new investors. The following table illustrates this per share dilution:

Assumed offering price per share	$4.50
Net tangible book value per share as of September 30, 2017	0.86
Increase per share attributable to new investors	1.34
As adjusted net tangible book value per share as of September 30, 2017, after giving effect to this offering	2.20
Dilution per share to new investors purchasing shares in this offering	2.30

The table above assumes for illustrative purposes that an aggregate of 16,666,666 of our common stock are sold pursuant to this prospectus supplement at a price of $4.50 per share, the last reported sale price of our common stock on the OTCQB on February 16, 2018, for aggregate gross proceeds of $75,000,000. The shares are being sold from time to time at various prices pursuant to the sales agreement with Cantor. An increase of $1.00 per share in the price at which the shares are sold from the assumed offering price of $4.50 per share shown in the table above, assuming all of our common stock in the aggregate amount of $75,000,000 is sold at that price, would increase our adjusted net tangible book value per share after the offering to $2.37 per share and would increase the dilution in net tangible book value per share to new investors in this offering to $3.13 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of $1.00 per share in the price at which the shares are sold from the assumed offering price of $4.50 per share shown in the table above, assuming all of our common stock in the aggregate amount of $75,000,000 is sold at that price, would decrease our adjusted net tangible book value per share after the offering to $1.99 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to $1.51 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The above discussion and table are based on 27,070,038 shares of common stock issued and outstanding as of September 30, 2017.

To the extent that options outstanding as of September 30, 2017, have been or are exercised, or other shares are issued, investors purchasing shares in this offering could experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

PLAN OF DISTRIBUTION

In accordance with the terms of our Controlled Equity Offering[SM] Sales Agreement, or the sales agreement, with Cantor Fitzgerald & Co., or Cantor, we may offer and sell our common stock from time to time through Cantor, acting as agent, having an aggregate offering price of up to $75,000,000. This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of our Controlled Equity Offering[SM] Sales Agreement that we entered into with Cantor is filed with the SEC as an exhibit to the registration statement of which this prospectus supplement is a part.

Cantor may sell the shares of common stock by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended. Subject to the terms of the placement notice, Cantor may also sell the shares of common stock by any other method permitted by law, including in privately negotiated transactions.

Each time we wish to issue and sell shares of common stock under the sales agreement, we will notify Cantor of the number of shares to be issued, the dates on which such sales are anticipated to be made and any minimum price below which sales may not be made. Once we have so instructed Cantor, unless it declines to accept the terms of this notice, Cantor has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Cantor under the sales agreement to sell our common stock are subject to a number of conditions that we must meet. We or Cantor may suspend the offering of our common stock upon notice and, subject to other conditions, our prior approval.

The settlement between us and Cantor is generally anticipated to occur on the second trading day following the date on which the sale was made, or on some other date that is agreed upon by us and Cantor in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Cantor may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Pursuant to the sales agreement, Cantor will be entitled to a commission up to an aggregate of 3.0% of the gross proceeds we receive from the sales of our shares of common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In connection with the sale of the shares of common stock on our behalf, Cantor will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of each sales agent will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Cantor with respect to certain civil liabilities, including liabilities under the Securities Act. We have also agreed to reimburse Cantor for certain specified expenses, including the fees and disbursements of its legal counsel in an amount not to exceed $50,000. We estimate that the total expenses for the offering, excluding compensation payable to the Cantor under the terms of the sales agreement, will be approximately $200,000.

The offering of common stock pursuant to the sales agreement and this prospectus supplement will terminate upon the termination of the sales agreement as permitted therein. We and Cantor may each terminate the sales agreement at any time upon 10 days' prior notice.

Cantor and its affiliates have in the past and may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they have or may in the future receive customary fees. To the extent required by Regulation M under the Exchange Act, Cantor will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement.

This prospectus supplement in electronic format may be made available on a website maintained by Cantor and Cantor may distribute this prospectus supplement and the accompanying base prospectus electronically.

LEGAL MATTERS

The validity of the common stock being offered hereby will be passed upon by Goodwin Procter LLP, Boston, Massachusetts. Cantor Fitzgerald & Co. is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited the financial statements of Aerpio Pharmaceuticals, Inc. at December 31, 2016 and 2015, and for each of the two years in the period ended December 31, 2016, as set forth in their report dated March 9, 2017 (except for the paragraphs included under the caption "Merger and Offering" described in Notes 1 and 15, as to which the date is May 22, 2017), included in the Aerpio Pharmaceuticals, Inc. Registration Statement (Form S-1 No. 333-217320) and incorporated by reference herein. The financial statements of Aerpio Pharmaceuticals, Inc. are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

LWBJ, LLP, independent registered accounting firm, has audited the financial statements of Zeta Acquisition Corp. II at December 31, 2015 and 2016, and for the years then ended, as set forth in their report dated March 7, 2017, included in the Aerpio Pharmaceuticals, Inc. Registration Statement (Form S-1 No. 333-217320) and incorporated by reference herein. The financial statements of Zeta Acquisition Corp. II are incorporated by reference in reliance on LWBJ, LLP's report, given on their authority as experts in accounting and auditing.

DOCUMENTS INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference the information we file with the SEC, by referring you to other documents filed separately with the SEC. The information incorporated by reference is considered to be part of this prospectus supplement. Any information that we file later with the SEC and that is deemed incorporated by reference will automatically update and supersede the information in this prospectus supplement. In all such cases, you should rely on the later information over different information included in this prospectus supplement or in any incorporated document. You should not assume that information in any document incorporated by reference into this prospectus supplement or any accompanying prospectus supplement is current as of any date other than the date of that document. This prospectus supplement will be deemed to incorporate by reference the following documents, except that we do not incorporate any document or portion of a document that was furnished and deemed by the rules of the SEC not to have been filed:

- Annual Report on Form 10-K for the year ended December 31, 2016;
- Quarterly Reports on Form 10-Q filed with the SEC for the quarters ended March 31, 2017, June 30, 2017 and September 30, 2017;
- Current Reports on Form 8-K filed with the SEC on March 13, 2017, March 17, 2017, June 29, 2017, July 31, 2017, August 8, 2017, October 10, 2017, November 14, 2017, and December 18, 2017; and
- Registration Statement on Form S-1 filed with the SEC on April 14, 2017, and declared effective on June 23, 2017.

We will also incorporate by reference any future filings made with the SEC under the Exchange Act after (i) the date of the initial registration statement and prior to the effectiveness of the registration statement and (ii) the date of this prospectus supplement and before the completion of the offering of the securities under the registration statement. In addition, we will incorporate by reference certain future materials furnished to the SEC on Form 8-K after the date of the initial registration statement, but only to the extent specifically indicated in those submissions or in a future prospectus supplement. Each subsequently filed Annual Report should be deemed to supersede entirely each earlier filed Annual Report and Reports on Form 8-K containing our quarterly

earnings releases and, unless explicitly stated otherwise, such earlier reports should not be deemed to be part of this prospectus supplement or any accompanying prospectus supplement and you should not rely upon statements made in those earlier periodic reports.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus supplement, including exhibits to these documents. You should direct any requests for documents to Investor Relations, Aerpio Pharmaceuticals, Inc., 9987 Carver Road, Cincinnati, OH 45242; telephone: (513) 985-1920.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other information with the SEC. You may read and copy the reports, proxy statements and other information that we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information about the operation of its Public Reference Room and for its prescribed rates to obtain copies of such material. The SEC also maintains an Internet site that contains reports, proxy and information statements and other information regarding registrants, like us, that file electronically with the SEC. The address of the SEC's Internet site is *www.sec.gov*. Our Internet site is *www.aerpio.com*. Information contained on our Internet site is not a part of this prospectus supplement.

This prospectus supplement is part of a registration statement that we have filed with the SEC. To see more detail, you should read the registration statement and the exhibits and schedules filed with, or incorporated by reference into, our registration statement.

This registration statement, including the exhibits contained or incorporated by reference therein, can be read at the SEC web site or at the SEC office referred to above. Any statement made or incorporated by reference in this prospectus supplement concerning the contents of any contract, agreement or other document is only a summary of the actual contract, agreement or other document. If we have filed or incorporated by reference any contract, agreement or other document as an exhibit to the registration statement, you should read the exhibit for a more complete understanding of the document or matter involved. Each statement regarding a contract, agreement or other document is qualified in its entirety by reference to the actual document.

Table of Contents

Up to $75,000,000

Common Stock

PROSPECTUS SUPPLEMENT

, 2018

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS
Part II—INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The expenses payable by us in connection with the issuance and distribution of the securities being registered (other than underwriting discounts and commissions, if any) are set forth below. Each item listed is estimated, except for the SEC registration fee and the FINRA filing fee.

Securities and Exchange Commission registration fee	$18,675
FINRA filing fee	$23,000
Legal fees and expenses	*
Accounting fees and expenses	*
Printing fees and expenses	*
Transfer agent and trustee fees	*
Miscellaneous	*
Total	$ *

* Estimated expenses not presently known. Each prospectus supplement will reflect estimated expenses based on the amount of the related offering.

Item 15. Indemnification of Directors and Officers

We are incorporated under the laws of the State of Delaware. Section 145 of the Delaware General Corporation Law provides that a Delaware corporation may indemnify any persons who were, are, or are threatened to be made, parties to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of such corporation), by reason of the fact that such person is or was an officer, director, employee or agent of such corporation, or is or was serving at the request of such corporation as an officer, director, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests and, with respect to any criminal action or proceeding, had no reasonable cause to believe that his or her conduct was illegal. A Delaware corporation may indemnify any persons who were, are, or are threatened to be made, a party to any threatened, pending or completed action or suit by or in the right of the corporation by reason of the fact that such person is or was a director, officer, employee or agent of such corporation, or is or was serving at the request of such corporation as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses (including attorneys' fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit provided such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the corporation's best interests except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to the corporation. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, the corporation must indemnify him or her against the expenses (including attorneys' fees) actually and reasonably incurred.

Our amended and restated certificate of incorporation and amended and restated bylaws provide for the indemnification of its directors and officers to the fullest extent permitted under the Delaware General Corporation Law.

Section 102(b)(7) of the Delaware General Corporation Law permits a corporation to provide in its certificate of incorporation that a director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duties as a director, except for liability for any:

- transaction from which the director derives an improper personal benefit;
- act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- breach of a director's duty of loyalty to the corporation or its stockholders.

Our amended and restated certificate of incorporation includes such a provision. Expenses incurred by any officer or director in defending any such action, suit or proceeding in advance of its final disposition shall be paid by us upon delivery to us of an undertaking, by or on behalf of such director or officer, to repay all amounts so advanced if it shall ultimately be determined that such director or officer is not entitled to be indemnified by us.

Section 174 of the Delaware General Corporation Law provides, among other things, that a director who willfully or negligently approves of an unlawful payment of dividends or an unlawful stock purchase or redemption may be held liable for such actions. A director who was either absent when the unlawful actions were approved, or dissented at the time, may avoid liability by causing his or her dissent to such actions to be entered in the books containing minutes of the meetings of the board of directors at the time such action occurred or immediately after such absent director receives notice of the unlawful acts.

As permitted by the Delaware General Corporation Law, we have entered into indemnity agreements with each of our directors and executive officers, that require us to indemnify such persons against any and all costs and expenses (including attorneys', witness or other professional fees) actually and reasonably incurred by such person in connection with any action, suit or proceeding (including derivative actions), whether actual or threatened, to which any such person may be made a party by reason of the fact that such person is or was a director or officer or is or was acting or serving as an officer, director, employee or agent of us or any of our affiliated enterprises, provided that such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to our best interests and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. The indemnification agreements also set forth certain procedures that will apply in the event of a claim for indemnification thereunder.

At present, there is no pending litigation or proceeding involving any of our directors or executive officers as to which indemnification is required or permitted, and we are not aware of any threatened litigation or proceeding that may result in a claim for indemnification.

We have an insurance policy in place that covers our officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, or otherwise.

Reference is made to the following documents listed as exhibits to this registration statement regarding relevant indemnification provisions described above and elsewhere herein:

Exhibit Document	Number
Amended and Restated Certificate of Incorporation.	3.2
Amended and Restated Bylaws.	3.3
Form of Indemnification Agreement.	10.4

Item 16. Exhibits

A list of exhibits filed with this registration statement on Form S-3 is set forth on the Exhibit Index and is incorporated herein by reference.

Item 17. Undertakings

The undersigned registrant hereby undertakes:

(a)(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement; provided, however, that paragraphs (a)(1)(i), (a)(l)(ii) and (a)(1) (iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering;

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(i) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and (ii) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(l)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date;

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary

offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser;

(6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

(7) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933 and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act of 1933 and will be governed by the final adjudication of such issue;

(8) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act of 1939 in accordance with the rules and regulations prescribed by the Securities and Exchange Commission under Section 305(b) (2) of the Trust Indenture Act of 1939.

EXHIBIT INDEX

Exhibit No.	Description
1.1*	Form of Underwriting Agreement
1.2	Controlled Equity Offering℠ Sales Agreement, dated February 21, 2018, by and between Aerpio Pharmaceuticals, Inc. and Cantor Fitzgerald & Co.
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
3.2	Amended and Restated By-laws of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.3 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
4.1	Specimen Stock Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-217320) filed April 14, 2017)
4.2	Registration Rights Agreement by and among Registrant, the Purchasers named therein, the Brokers named therein and the other individuals named therein, dated March 15, 2017 (incorporated by reference to Exhibit 10.5 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
4.3	Registration Rights Agreement by and among Registrant and the Investors named therein, dated March 15, 2017 (incorporated by reference to Exhibit 10.9 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
4.4	Form of Warrant Agreements (incorporated by reference to Exhibit 4.1 to the Registrant's Form 8-K filed with the Securities and Exchange Commission March 17, 2017, File No. 000-53057)
4.5	Form of indenture for subordinated debt securities and the related form of subordinated debt security
4.6	Form of indenture for senior debt securities and the related form of senior debt security
4.7*	Form of Preferred Stock Certificate
4.8*	Form of Warrant Agreement
4.9*	Form of Unit Agreement
5.1	Opinion of Goodwin Procter LLP (relating to the base prospectus)
5.2	Opinion of Goodwin Procter LLP (relating to the prospectus supplement)
12.1	Computation of Ratio of Earnings to Fixed Charges
23.1	Consent of Ernst & Young LLP
23.2	Consent of LWBJ, LLP
23.3	Consent of Goodwin Procter LLP (included in Exhibits 5.1 and 5.2 hereto)
24.1	Power of Attorney (included on the signature pages to this registration statement)
25.1**	Form T-1 Statement of Eligibility of Trustee for Senior Indenture under the Trust Indenture Act of 1939
25.2**	Form T-1 Statement of Eligibility of Trustee for Subordinated Indenture under the Trust Indenture Act of 1939

* To be filed by amendment or by a Current Report on Form 8-K.
** To be filed pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cincinnati, State of Ohio, on the 21st day of February, 2018.

AERPIO PHARMACEUTICALS, INC.

By: /s/ Stephen Hoffman, M.D., Ph.D.
Stephen Hoffman, M.D., Ph.D.
Chief Executive Officer and Principal Executive Officer

POWER OF ATTORNEY

Each person whose individual signature appears below hereby authorizes and appoints Stephen Hoffman and Michael Rogers and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney in fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Registration Statement, including any and all post effective amendments and amendments thereto, and any registration statement relating to the same offering as this Registration Statement that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys in fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys in fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement and Power of Attorney has been signed by the following person in the capacities and on the date indicated.

Name	Title	Date
/s/ Stephen Hoffman, M.D., Ph.D. Stephen Hoffman, M.D., Ph.D.	Director, Chief Executive Officer and Principal Executive Officer	February 21, 2018
/s/ Michael Rogers Michael Rogers	Chief Financial Officer and Principal Financial and Accounting Officer	February 21, 2018
/s/ Joseph Gardner Joseph Gardner	Director, President and Founder	February 21, 2018
/s/ Muneer A. Satter Muneer A. Satter	Director	February 21, 2018
/s/ Chau Khuong Chau Khuong	Director	February 21, 2018
/s/ Steven Prelack Steven Prelack	Director	February 21, 2018
/s/ Paul Weiss Paul Weiss	Director	February 21, 2018
/s/ Caley Castelein Caley Castelein	Director	February 21, 2018
/s/ Anupam Dalal Anupam Dalal	Director	February 21, 2018
/s/ Pravin Dugel Pravin Dugel	Director	February 21, 2018

Exhibit 1.2

AERPIO PHARMACEUTICALS, INC.

Shares of Common Stock
(par value $0.0001 per share)

Controlled Equity Offering[SM]

Sales Agreement

February 21, 2018

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022

Ladies and Gentlemen:

Aerpio Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), confirms its agreement (this "**Agreement**") with Cantor Fitzgerald & Co. (the "**Agent**"), as follows:

1. Issuance and Sale of Shares. The Company agrees that, from time to time during the term of this Agreement, on the terms and subject to the conditions set forth herein, it may issue and sell through the Agent, shares of common stock (the "**Placement Shares**") of the Company, par value $0.0001 per share (the "**Common Stock**"); *provided*, *however*, that in no event shall the Company issue or sell through the Agent such number or dollar amount of Placement Shares that would (a) exceed the number or dollar amount of shares of Common Stock registered on the effective Registration Statement (defined below) pursuant to which the offering is being made, (b) exceed the number of authorized but unissued shares of Common Stock (less shares of Common Stock issuable upon exercise, conversion or exchange of any outstanding securities of the Company or otherwise reserved from the Company's authorized capital stock), (c) exceed the number or dollar amount of shares of Common Stock permitted to be sold under Form S-3 (including General Instruction I.B.6 thereof, if applicable) or (d) exceed the number or dollar amount of shares of Common Stock for which the Company has filed a Prospectus Supplement (as defined below) (the lesser of (a), (b), (c) and (d), the "**Maximum Amount**"). Notwithstanding anything to the contrary contained herein, the parties hereto agree that compliance with the limitations set forth in this Section 1 on the amount of Placement Shares issued and sold under this Agreement shall be the sole responsibility of the Company and that the Agent shall have no obligation in connection with such compliance. The offer and sale of Placement Shares through the Agent will be effected pursuant to the Registration Statement (as defined below) filed by the Company and which will be declared effective by the Securities and Exchange Commission (the "**Commission**"), although nothing in this Agreement shall be construed as requiring the Company to use the Registration Statement to issue Common Stock.

The Company has filed or will file, in accordance with the provisions of the Securities Act of 1933, as amended (the "**Securities Act**") and the rules and regulations thereunder (the "**Securities Act Regulations**"), with the Commission a registration statement on Form S-3, including a base prospectus, relating to certain securities, including the Placement Shares to be issued from time to time by the Company, and which incorporates by reference documents that

the Company has filed or will file in accordance with the provisions of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and the rules and regulations thereunder. The Company has prepared a prospectus or a prospectus supplement to the base prospectus included as part of the registration statement, which prospectus or prospectus supplement relates to the Placement Shares to be issued from time to time by the Company (the "**Prospectus Supplement**"). The Company will furnish to the Agent, for use by the Agent, copies of the prospectus included as part of such registration statement, as supplemented, by the Prospectus Supplement, relating to the Placement Shares to be issued from time to time by the Company. The Company may file one or more additional registration statements from time to time that will contain a base prospectus and related prospectus or prospectus supplement, if applicable (which shall be a Prospectus Supplement), with respect to the Placement Shares. Except where the context otherwise requires, such registration statement(s), including all documents filed as part thereof or incorporated by reference therein, and including any information contained in a Prospectus (as defined below) subsequently filed with the Commission pursuant to Rule 424(b) under the Securities Act Regulations or deemed to be a part of such registration statement pursuant to Rule 430B of the Securities Act Regulations, is herein called the "**Registration Statement**." The base prospectus or base prospectuses, including all documents incorporated therein by reference, included in the Registration Statement, as it may be supplemented, if necessary, by the Prospectus Supplement, in the form in which such prospectus or prospectuses and/or Prospectus Supplement have most recently been filed by the Company with the Commission pursuant to Rule 424(b) under the Securities Act Regulations, together with the then issued Issuer Free Writing Prospectus(es) (as defined below), is herein called the "**Prospectus**."

Any reference herein to the Registration Statement, any Prospectus Supplement, Prospectus or any Issuer Free Writing Prospectus shall be deemed to refer to and include the documents, if any, incorporated by reference therein (the "**Incorporated Documents**"), including, unless the context otherwise requires, the documents, if any, filed as exhibits to such Incorporated Documents. Any reference herein to the terms "amend," "amendment" or "supplement" with respect to the Registration Statement, any Prospectus Supplement, the Prospectus or any Issuer Free Writing Prospectus shall be deemed to refer to and include the filing of any document under the Exchange Act on or after the most-recent effective date of the Registration Statement, or the date of the Prospectus Supplement, Prospectus or such Issuer Free Writing Prospectus, as the case may be, and incorporated therein by reference. For purposes of this Agreement, all references to the Registration Statement, the Prospectus or to any amendment or supplement thereto shall be deemed to include the most recent copy filed with the Commission pursuant to its Electronic Data Gathering Analysis and Retrieval system, or if applicable, the Interactive Data Electronic Application system when used by the Commission (collectively, "**EDGAR**").

2. Placements. Each time that the Company, in its sole discretion, wishes to issue and sell Placement Shares hereunder (each, a "**Placement**"), it will notify the Agent by email notice (or other method mutually agreed to in writing by the parties) of the number of Placement Shares to be issued, the time period during which sales are requested to be made, any limitation on the number of Placement Shares that may be sold in any one day and any minimum price below which sales may not be made (a "**Placement Notice**"), the form of which is attached hereto as Schedule 1. The Placement Notice shall originate from any of the individuals from the Company set forth on Schedule 3 (with a copy to each of the other individuals from the

Company listed on such schedule), and shall be addressed to each of the individuals from the Agent set forth on Schedule 3, as such Schedule 3 may be amended from time to time. The Placement Notice shall be effective unless and until (i) the Agent declines in writing or by email to accept the terms contained therein for any reason, in its sole discretion, within two (2) Business Day (as defined below) of receipt of such Placement Notice, (ii) the entire amount of the Placement Shares thereunder have been sold, (iii) the Company suspends or terminates the Placement Notice or (iv) this Agreement has been terminated under the provisions of Section 12. The amount of any discount, commission or other compensation to be paid by the Company to Agent in connection with the sale of the Placement Shares shall be calculated in accordance with the terms set forth in Schedule 2. It is expressly acknowledged and agreed that neither the Company nor the Agent will have any obligation whatsoever with respect to a Placement or any Placement Shares unless and until the Company delivers a Placement Notice to the Agent and the Agent does not decline such Placement Notice pursuant to the terms set forth above, and then only upon the terms specified therein and herein. In the event of a conflict between the terms of this Agreement and the terms of a Placement Notice, the terms of the Placement Notice will control; provided that in no event shall the sale of the Placement Shares in accordance with such Placement Notice exceed the Maximum Amount.

3. Sale of Placement Shares by Agent. Subject to the provisions of Section 5(a), the Agent, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable state and federal laws, rules and regulations and the rules of the applicable Nasdaq stock market (the "**Exchange**"), to sell the Placement Shares up to the amount specified, and otherwise in accordance with the terms of such Placement Notice. The Agent will provide written confirmation to the Company no later than the opening of the Trading Day (as defined below) immediately following the Trading Day on which it has made sales of Placement Shares hereunder setting forth the number of Placement Shares sold on such day, the compensation payable by the Company to the Agent pursuant to Section 2 with respect to such sales, and the Net Proceeds (as defined below) payable to the Company, with an itemization of the deductions made by the Agent (as set forth in Section 5(b)) from the gross proceeds that it receives from such sales. Subject to the terms of the Placement Notice, the Agent may sell Placement Shares by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) of the Securities Act Regulations, including sales made directly on or through the Exchange or any other existing trading market for the Common Stock, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices and/or any other method permitted by law. "**Trading Day**" means any day on which Common Stock is traded on the Exchange.

4. Suspension of Sales. The Company or the Agent may, upon notice to the other party in writing (including by email correspondence to each of the individuals of the other party set forth on Schedule 3, if receipt of such correspondence is actually acknowledged by any of the individuals to whom the notice is sent, other than via auto-reply) or by telephone (confirmed immediately by verifiable facsimile transmission or email correspondence to each of the individuals of the other party set forth on Schedule 3), suspend any sale of Placement Shares (a "**Suspension**"); *provided*, *however*, that such Suspension shall not affect or impair any party's obligations with respect to any Placement Shares sold hereunder prior to the receipt of such notice. While a Suspension is in effect any obligation under Sections 7(l), 7(m), and 7(n) with

respect to the delivery of certificates, opinions, or comfort letters to the Agent, shall be waived. Each of the parties agrees that no such notice under this Section 4 shall be effective against any other party unless it is made to one of the individuals named on Schedule 3 hereto, as such Schedule may be amended from time to time.

5. Sale and Delivery to the Agent; Settlement.

(a) Sale of Placement Shares. On the basis of the representations and warranties herein contained and subject to the terms and conditions herein set forth, upon the Agent's acceptance of the terms of a Placement Notice, and unless the sale of the Placement Shares described therein has been declined, suspended, or otherwise terminated in accordance with the terms of this Agreement, the Agent, for the period specified in the Placement Notice, will use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable law and regulations to sell such Placement Shares up to the amount specified, and otherwise in accordance with the terms of such Placement Notice. The Company acknowledges and agrees that (i) there can be no assurance that the Agent will be successful in selling Placement Shares, (ii) the Agent will incur no liability or obligation to the Company or any other person or entity if it does not sell Placement Shares for any reason other than a failure by the Agent to use its commercially reasonable efforts consistent with its normal trading and sales practices and applicable law and regulations to sell such Placement Shares as required under this Agreement and (iii) the Agent shall be under no obligation to purchase Placement Shares on a principal basis pursuant to this Agreement, except as otherwise agreed by the Agent and the Company.

(b) Settlement of Placement Shares. Unless otherwise specified in the applicable Placement Notice, settlement for sales of Placement Shares will occur on the second (2nd) Trading Day (or such earlier day as is industry practice for regular-way trading) following the date on which such sales are made (each, a "**Settlement Date**"). The Agent shall notify the Company of each sale of Placement Shares no later than the opening of the Trading Day immediately following the Trading Day on which it has made sales of Placement Shares hereunder. The amount of proceeds to be delivered to the Company on a Settlement Date against receipt of the Placement Shares sold (the "**Net Proceeds**") will be equal to the aggregate sales price received by the Agent, after deduction for (i) the Agent's commission, discount or other compensation for such sales payable by the Company pursuant to Section 2 hereof, and (ii) any transaction fees imposed by any Governmental Authority in respect of such sales.

(c) Delivery of Placement Shares. On or before each Settlement Date, the Company will, or will cause its transfer agent to, electronically transfer the Placement Shares being sold by crediting the Agent's or its designee's account (provided the Agent shall have given the Company written notice of such designee at least one Trading Day prior to the Settlement Date) at The Depository Trust Company through its Deposit and Withdrawal at Custodian System or by such other means of delivery as may be mutually agreed upon by the parties hereto which in all cases shall be freely tradable, transferable, registered shares in good deliverable form. On each Settlement Date, the Agent will deliver the related Net Proceeds in same day funds to an account designated by the Company on, or prior to, the Settlement Date. The Company agrees that if the Company, or its transfer agent (if applicable), defaults in its obligation to deliver Placement Shares on a Settlement Date, the Company agrees that in addition to and in no way limiting the rights and obligations set forth in Section 10(a) hereto, it

will (i) hold the Agent harmless against any loss, claim, damage, or expense (including reasonable legal fees and expenses), as incurred, arising out of or in connection with such default by the Company or its transfer agent (if applicable) and (ii) pay to the Agent any commission, discount, or other compensation to which it would otherwise have been entitled absent such default.

(d) Denominations; Registration. Certificates for the Placement Shares, if any, shall be in such denominations and registered in such names as the Agent may request in writing at least one full Business Day (as defined below) before the Settlement Date. The certificates for the Placement Shares, if any, will be made available by the Company for examination and packaging by the Agent in The City of New York not later than noon (New York time) on the Business Day prior to the Settlement Date.

(e) Limitations on Offering Size. Under no circumstances shall the Company cause or request the offer or sale of any Placement Shares if, after giving effect to the sale of such Placement Shares, the aggregate gross sales proceeds of Placement Shares sold pursuant to this Agreement would exceed the lesser of (A) together with all sales of Placement Shares under this Agreement, the Maximum Amount, and (B) the amount authorized from time to time to be issued and sold under this Agreement by the Company's board of directors, a duly authorized committee thereof or a duly authorized executive committee, and notified to the Agent in writing. Under no circumstances shall the Company cause or request the offer or sale of any Placement Shares pursuant to this Agreement at a price lower than the minimum price authorized from time to time by the Company's board of directors, a duly authorized committee thereof or a duly authorized executive committee. Further, under no circumstances shall the Company cause or permit the aggregate offering amount of Placement Shares sold pursuant to this Agreement to exceed the Maximum Amount.

6. Representations and Warranties of the Company. The Company represents and warrants to, and agrees with Agent that as of the date of this Agreement and as of each Applicable Time (as defined below), unless such representation or warranty specifies a different time:

(a) Registration Statement and Prospectus. The Company and the transactions contemplated by this Agreement meet the requirements for and comply with the applicable conditions set forth in Form S-3 (including General Instructions I.A and I.B) under the Securities Act. The Registration Statement has been or will be filed with the Commission and will be declared effective by the Commission under the Securities Act prior to the issuance of any Placement Notices by the Company. The Prospectus Supplement will name the Agent as the agent in the section entitled "Plan of Distribution." The Company has not received, and has no notice of, any order of the Commission preventing or suspending the use of the Registration Statement, or threatening or instituting proceedings for that purpose. The Registration Statement and the offer and sale of Placement Shares pursuant to this Agreement hereby meet the requirements of Rule 415 under the Securities Act and comply in all material respects with said Rule. Any statutes, regulations, contracts or other documents that are required to be described in the Registration Statement or the Prospectus or to be filed as exhibits to the Registration Statement have been or will be so described or filed prior to the issuance of any Placement Notices by the Company. Copies of the Registration Statement, the Prospectus, and any such amendments or supplements and all Incorporated Documents that were filed with the

Commission on or prior to the date of this Agreement have been delivered, or are available through EDGAR, to Agent and its counsel. The Company has not distributed and, prior to the later to occur of each Settlement Date and completion of the distribution of the Placement Shares, will not distribute any offering material in connection with the offering or sale of the Placement Shares other than the Registration Statement and the Prospectus and any Issuer Free Writing Prospectus (as defined below) to which the Agent has consented, any such consent not to be unreasonably withheld, conditioned or delayed. The Common Stock is or will be registered pursuant to Section 12(b) of the Exchange Act and is or will be listed on the Exchange under the trading symbol "ARPO." The Company has taken no action designed to, or likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act, delisting the Common Stock from the Exchange, nor has the Company received any notification that the Commission or the Exchange is contemplating terminating such registration or listing. To the Company's knowledge, it is in compliance with all applicable listing requirements of the Exchange.

(b) No Misstatement or Omission. The Registration Statement, when it became or becomes effective, and the Prospectus, and any amendment or supplement thereto, on the date of such Prospectus or amendment or supplement, conformed and will conform in all material respects with the requirements of the Securities Act. At each Settlement Date, the Registration Statement and the Prospectus, as of such date, will conform in all material respects with the requirements of the Securities Act. The Registration Statement, when it became or becomes effective, did not, and will not, contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. The Prospectus and any amendment and supplement thereto, on the date thereof and at each Applicable Time (defined below), did not or will not include an untrue statement of a material fact or omit to state a material fact necessary to make the statements therein, in light of the circumstances under which they were made, not misleading. The Incorporated Documents did not, and any further Incorporated Documents filed after the date of this Agreement will not, when filed with the Commission, contain an untrue statement of a material fact or omit to state a material fact required to be stated in such document or necessary to make the statements in such document, in light of the circumstances under which they were made, not misleading. The foregoing shall not apply to statements in, or omissions from, any such document made in reliance upon, and in conformity with, information furnished to the Company by Agent specifically for use in the preparation thereof.

(c) Conformity with Securities Act and Exchange Act. The Registration Statement, the Prospectus, any Issuer Free Writing Prospectus or any amendment or supplement thereto, and the Incorporated Documents , when such documents were or are filed with the Commission under the Securities Act or the Exchange Act or became or become effective under the Securities Act, as the case may be, conformed or will conform in all material respects with the requirements of the Securities Act and the Exchange Act, as applicable.

(d) Financial Information. The consolidated financial statements of the Company included or incorporated by reference in the Registration Statement, the Prospectus and the Issuer Free Writing Prospectuses, if any, together with the related notes and schedules, present fairly, in all material respects, the consolidated financial position of the Company and the Subsidiaries (as defined below) as of the dates indicated and the consolidated results of

operations, cash flows and changes in stockholders' equity of the Company for the periods specified and have been prepared in compliance with the requirements of the Securities Act and Exchange Act and in conformity with GAAP (as defined below) applied on a consistent basis during the periods involved; the summary and selected financial data with respect to the Company and the Subsidiaries (as defined below) contained or incorporated by reference in the Registration Statement, the Prospectus and the Issuer Free Writing Prospectuses, if any, are accurately and fairly presented and prepared on a basis consistent with the financial statements and accounting books and records of the Company; there are no financial statements (historical or pro forma) that are required to be included or incorporated by reference in the Registration Statement, or the Prospectus that are not included or incorporated by reference as required; the Company and the Subsidiaries (as defined below) do not have any material liabilities or obligations, direct or contingent (including any off-balance sheet obligations), not described in the Registration Statement (excluding the exhibits thereto) and the Prospectus; and all disclosures contained or incorporated by reference in the Registration Statement, the Prospectus and the Issuer Free Writing Prospectuses, if any, regarding "non-GAAP financial measures" (as such term is defined by the rules and regulations of the Commission) comply, in all material respects, with Regulation G of the Exchange Act and Item 10 of Regulation S-K under the Securities Act, to the extent applicable. The interactive data in eXtensible Business Reporting Language included or incorporated by reference in the Registration Statement and the Prospectus fairly presents the information called for in all material respects and has been prepared in accordance with the Commission's rules and guidelines applicable thereto.

(e) Conformity with EDGAR Filing. The Prospectus delivered to Agent for use in connection with the sale of the Placement Shares pursuant to this Agreement will be identical to the versions of the Prospectus created to be transmitted to the Commission for filing via EDGAR, except to the extent permitted by Regulation S-T.

(f) Organization. The Company and each of its Subsidiaries are duly organized, validly existing as a corporation or a company and in good standing under the laws of their respective jurisdictions of organization. The Company and each of its Subsidiaries are duly licensed or qualified as a foreign corporation for transaction of business and in good standing under the laws of each other jurisdiction in which their respective ownership or lease of property or the conduct of their respective businesses requires such license or qualification, and have all corporate power and authority necessary to own or hold their respective properties and to conduct their respective businesses as described in the Registration Statement and the Prospectus, except where the failure to be so qualified or in good standing or have such power or authority would not, individually or in the aggregate, have a material adverse effect or would reasonably be expected to have a material adverse effect on or affecting the assets, business, operations, earnings, properties, condition (financial or otherwise), prospects, stockholders' equity or results of operations of the Company and the Subsidiaries taken as a whole, or prevent or materially interfere with consummation of the transactions contemplated hereby (a "**Material Adverse Effect**").

(g) Subsidiaries. The subsidiaries set forth on Schedule 4 (collectively, the "**Subsidiaries**"), are the Company's only significant subsidiaries (as such term is defined in Rule 1-02 of Regulation S-X promulgated by the Commission). Except as set forth in the Registration Statement and in the Prospectus, the Company owns, directly or indirectly, all of the equity

interests of the Subsidiaries free and clear of any lien, charge, security interest, encumbrance, right of first refusal or other restriction, and all the equity interests of the Subsidiaries are validly issued and are fully paid, nonassessable and free of preemptive and similar rights. No Subsidiary is currently prohibited, directly or indirectly, from paying any dividends to the Company, from making any other distribution on such Subsidiary's capital stock, from repaying to the Company any loans or advances to such Subsidiary from the Company or from transferring any of such Subsidiary's property or assets to the Company or any other Subsidiary of the Company.

(h) No Violation or Default. Neither the Company nor any of its Subsidiaries is (i) in violation of its charter or by-laws or similar organizational documents; (ii) in default, and no event has occurred that, with notice or lapse of time or both, would constitute such a default, in the due performance or observance of any term, covenant or condition contained in any indenture, mortgage, deed of trust, loan agreement or other agreement or instrument to which the Company or any of its Subsidiaries is a party or by which the Company or any of its Subsidiaries is bound or to which any of the property or assets of the Company or any of its Subsidiaries are subject; or (iii) in violation of any law or statute or any judgment, order, rule or regulation of any Governmental Authority, except, in the case of each of clauses (ii) and (iii) above, for any such violation or default that would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect. To the Company's knowledge, no other party under any material contract or other agreement to which it or any of its Subsidiaries is a party is in default in any respect thereunder where such default would have a Material Adverse Effect.

(i) No Material Adverse Change. Subsequent to the respective dates as of which information is given in the Registration Statement, the Prospectus and the Free Writing Prospectuses, if any (including any Incorporated Document), there has not been (i) any Material Adverse Effect or the occurrence of any development that the Company reasonably expects will result in a Material Adverse Effect, (ii) other than as contemplated by this Agreement, any transaction which is material to the Company and the Subsidiaries taken as a whole, (iii) any obligation or liability, direct or contingent (including any off-balance sheet obligations), incurred by the Company or any Subsidiary, which is material to the Company and the Subsidiaries taken as a whole, (iv) any material change in the capital stock (other than as a result of the sale of Placement Shares) or outstanding long-term indebtedness of the Company or any of its Subsidiaries or (v) any dividend or distribution of any kind declared, paid or made on the capital stock of the Company or any Subsidiary, other than in each case above in the ordinary course of business or as otherwise disclosed in the Registration Statement or Prospectus (including any document deemed incorporated by reference therein).

(j) Capitalization. The issued and outstanding shares of capital stock of the Company have been validly issued, are fully paid and nonassessable and, other than as disclosed in the Registration Statement or the Prospectus, are not subject to any preemptive rights, rights of first refusal or similar rights pursuant to the Company's charter, bylaws, applicable law or any agreement or other instrument to which the Company is a party or by which the Company is bound. The Company has an authorized, issued and outstanding capitalization as set forth in the Registration Statement and the Prospectus as of the dates referred to therein (other than the grant of additional options under the Company's existing stock option plans or the sale of sales under the Company's existing employee stock purchase plan, or changes in the number of outstanding shares of Common Stock of the Company due to the issuance of shares upon the exercise or

conversion of securities exercisable for, or convertible into, Common Stock outstanding on the date hereof) and such authorized capital stock conforms in all material respects to the description thereof set forth in the Registration Statement and the Prospectus. The description of the securities of the Company in the Registration Statement and the Prospectus is complete and accurate in all material respects. Except as disclosed in or contemplated by the Registration Statement or the Prospectus, as of the date referred to therein, the Company does not have outstanding any options to purchase, or any rights or warrants to subscribe for, or any securities or obligations convertible into, or exchangeable for, or any contracts or commitments to issue or sell, any shares of capital stock or other securities (other than as a result of the grant of stock options under the Company's existing equity incentive plans after the date(s) set forth in the Registration Statement and the Prospectus).

(k) Authorization; Enforceability. The Company has full legal right, power and authority to enter into this Agreement and perform the transactions contemplated hereby. This Agreement has been duly authorized, executed and delivered by the Company and constitutes a legal, valid and binding agreement of the Company enforceable in accordance with its terms, except as rights to indemnification or contribution hereunder may be limited by federal or state securities laws and except as such enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' rights generally and by general equitable principles.

(l) Authorization of Placement Shares. The Placement Shares, when issued and delivered pursuant to the terms approved by the board of directors of the Company or a duly authorized committee thereof, or a duly authorized executive committee, against payment therefor as provided herein, will be duly and validly authorized and issued and fully paid and nonassessable, free and clear of any pledge, lien, encumbrance, security interest or other claim, including any statutory or contractual preemptive rights, resale rights, rights of first refusal or other similar rights, and will be registered pursuant to Section 12 of the Exchange Act. The Placement Shares, when issued, will conform in all material respects to the description of the Placement Shares contained in the Registration Statement and the Prospectus under the caption "Description of Capital Stock".

(m) No Consents Required. No consent, approval, authorization, order, registration or qualification of or with any Governmental Authority is required for the execution, delivery and performance by the Company of this Agreement, the issuance and sale by the Company of the Placement Shares, except for (i) the registration of the Placement Shares under the Securities Act; and (ii) such consents, approvals, authorizations, orders and registrations or qualifications as may be required under applicable state securities laws or by the by-laws and rules of the Financial Industry Regulatory Authority ("**FINRA**") or the Exchange in connection with the sale of the Placement Shares by the Agent.

(n) No Preferential Rights. Except as set forth in the Registration Statement and the Prospectus, (i) no person, as such term is defined in Rule 1-02 of Regulation S-X promulgated under the Securities Act (each, a "**Person**"), has the right, contractual or otherwise, to cause the Company to issue or sell to such Person any Common Stock or shares of any other capital stock or other securities of the Company, (ii) no Person has any preemptive rights, resale rights, rights of first refusal, rights of co-sale, or any other rights (whether pursuant to a "poison pill" provision or otherwise) to purchase any Common Stock or shares of any other capital stock

or other securities of the Company, (iii) no Person has the right to act as an underwriter or as a financial advisor to the Company in connection with the offer and sale of the Placement Shares, and (iv) no Person has the right, contractual or otherwise, to require the Company to register under the Securities Act any Common Stock or shares of any other capital stock or other securities of the Company, or to include any such shares or other securities in the Registration Statement or the offering contemplated thereby, whether as a result of the filing or effectiveness of the Registration Statement or the sale of the Placement Shares as contemplated thereby or otherwise.

(o) Independent Public Accounting Firm. Ernst & Young LLP (the "**Accountant**"), whose report on the consolidated financial statements of the Company is filed with the Commission as part of the Registration Statement and the Prospectus or the Company's most recent Annual Report on Form 10-K incorporated by reference into the Registration Statement and the Prospectus, are and, during the periods covered by their report, were an independent registered public accounting firm within the meaning of the Securities Act and the Public Company Accounting Oversight Board (United States). To the Company's knowledge, the Accountant is not in violation of the auditor independence requirements of the Sarbanes-Oxley Act of 2002 (the "**Sarbanes-Oxley Act**") with respect to the Company.

(p) Enforceability of Agreements. All agreements between the Company and third parties expressly referenced in the Prospectus, other than such agreements that have expired by their terms or the termination of which is disclosed in documents filed by the Company on EDGAR, are legal, valid and binding obligations of the Company enforceable in accordance with their respective terms, except to the extent that (i) enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' rights generally and by general equitable principles , (ii) the indemnification provisions of certain agreements may be limited by federal or state securities laws or public policy considerations in respect thereof, and (iii) any unenforceability, individually or in the aggregate, would not have a Material Adverse Effect.

(q) No Litigation. Except as set forth in the Registration Statement or the Prospectus, there are no actions, suits or proceedings by or before any Governmental Authority pending, nor, to the Company's knowledge, any audits or investigations by or before any Governmental Authority, to which the Company or a Subsidiary is a party or to which any property of the Company or any of its Subsidiaries is the subject that, individually or in the aggregate, if determined adversely to the Company or any of its Subsidiaries, would have a Material Adverse Effect and, to the Company's knowledge, no such actions, suits, proceedings, audits or investigations are threatened or contemplated by any Governmental Authority or threatened by others that, individually or in the aggregate would have a Material Adverse Effect; and (i) there are no current or pending audits, investigations, actions, suits or proceedings by or before any Governmental Authority that are required under the Securities Act to be described in the Prospectus that are not so described; and (ii) there are no contracts or other documents that are required under the Securities Act to be filed as exhibits to the Registration Statement that are not so filed.

(r) Consents and Permits. Except as disclosed in the Registration Statement and the Prospectus, the Company and its Subsidiaries have made all filings, applications and submissions required by, possesses and is operating in compliance with, all approvals, licenses,

certificates, certifications, clearances, consents, grants, exemptions, marks, notifications, orders, permits and other authorizations issued by, the appropriate federal, state or foreign Governmental Authority (including, without limitation, the United States Food and Drug Administration (the "**FDA**"), the United States Drug Enforcement Administration or any other foreign, federal, state, provincial, court or local government or regulatory authorities including self-regulatory organizations engaged in the regulation of clinical trials, pharmaceuticals, biologics or biohazardous substances or materials) necessary for the ownership or lease of their respective properties or to conduct its businesses as described in the Registration Statement and the Prospectus (collectively, "**Permits**"), except for such Permits the failure of which to possess, obtain or make the same would not reasonably be expected to have a Material Adverse Effect; the Company and its Subsidiaries are in compliance with the terms and conditions of all such Permits, except where the failure to be in compliance would not reasonably be expected to have a Material Adverse Effect; all of the Permits are valid and in full force and effect, except where any invalidity, individually or in the aggregate, would not be reasonably expected to have a Material Adverse Effect; and neither the Company nor any of its Subsidiaries has received any written notice from FDA, or other state, local or foreign Governmental Authority relating to the limitation, revocation, cancellation, suspension, modification or non-renewal of any such Permit which, individually or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would be reasonably expected to have a Material Adverse Effect, or has any reason to believe that any such license, certificate, permit or authorization will not be renewed in the ordinary course. To the extent required by applicable laws and regulations of the FDA, the Company or the applicable Subsidiary has submitted to the FDA an Investigational New Drug Application or amendment or supplement thereto for each clinical trial it has conducted or sponsored or is conducting or sponsoring in the United States; all such submissions were in material compliance with applicable laws and regulations when submitted and no material deficiencies have been asserted by the FDA with respect to any such submissions.

(s) Regulatory Filings. Except as disclosed in the Registration Statement and the Prospectus, neither the Company nor any of its Subsidiaries has failed to file with the applicable Governmental Authorities (including, without limitation, the FDA, or any foreign, federal, state, provincial or local Governmental Authority performing functions similar to those performed by the FDA) any required filing, declaration, listing, registration, report or submission, except for such failures that, individually or in the aggregate, would not reasonably be expected to have a Material Adverse Effect; except as disclosed in the Registration Statement and the Prospectus, all such filings, declarations, listings, registrations, reports or submissions were in compliance with applicable laws when filed and no deficiencies have been asserted by any applicable regulatory authority with respect to any such filings, declarations, listings, registrations, reports or submissions, except for any deficiencies that, individually or in the aggregate, would not reasonably be expected to have a Material Adverse Effect. The Company has operated and currently is, in all material respects, in compliance with the United States Federal Food, Drug, and Cosmetic Act, all applicable rules and regulations of the FDA and other federal, state, local and foreign Governmental Authority exercising comparable authority. The Company has no knowledge of any studies or trials not described in the Prospectus the results of which reasonably call into question in any material respect the results of the studies and trials described in the Prospectus.

(t) Intellectual Property. Except as disclosed in the Registration Statement and the Prospectus, the Company and its Subsidiaries own, possess, license or have other rights to use all foreign and domestic patents, patent applications, trade and service marks, trade and service mark registrations, trade names, copyrights, licenses, inventions, trade secrets, technology, Internet domain names, know-how and other intellectual property (collectively, the "**Intellectual Property**"), necessary for the conduct of their respective businesses as now conducted except to the extent that the failure to own, possess, license or otherwise hold adequate rights to use such Intellectual Property would not, individually or in the aggregate, have a Material Adverse Effect. Except as disclosed in the Registration Statement and the Prospectus (i) to the Company's knowledge, there are no rights of third parties to any material Intellectual Property owned by the Company and its Subsidiaries; (ii) to the Company's knowledge, there is no infringement by third parties of any such Intellectual Property owned by the Company and its Subsidiaries; (iii) there is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others challenging the Company's and its Subsidiaries' rights in or to any such Intellectual Property, and the Company is unaware of any facts which could form a reasonable basis for any such action, suit, proceeding or claim; (iv) there is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property; (v) there is no pending or, to the Company's knowledge, threatened action, suit, proceeding or claim by others that the Company and its Subsidiaries infringe or otherwise violate any patent, trademark, copyright, trade secret or other proprietary rights of others; (vi) to the Company's knowledge, there is no third-party U.S. patent or published U.S. patent application which contains claims for which an Interference Proceeding (as defined in 35 U.S.C. § 135) has been commenced against any patent or patent application described in the Prospectus as being owned by or licensed to the Company; and (vii) the Company and its Subsidiaries have complied with the terms of each agreement pursuant to which Intellectual Property has been licensed to the Company or such Subsidiary, and, to the Company's knowledge, all such agreements are in full force and effect, except, in the case of any of clauses (i)-(vii) above, for any such infringement by third parties or any such pending or threatened suit, action, proceeding or claim as would not, individually or in the aggregate, result in a Material Adverse Effect.

(u) Clinical Studies. To the Company's knowledge, the preclinical studies and clinical trials conducted or sponsored by the Company and described in the Prospectus were, and, if still pending, are being conducted in all material respects in accordance with the experimental protocols, procedures and controls pursuant to, where applicable, accepted professional and scientific standards for products or product candidates comparable to those being developed by the Company; the descriptions of such studies and trials, and the results thereof, contained in the Prospectus are accurate and complete in all material respects; the Company is not aware of any studies or trials not described in the Prospectus, the results of which reasonably call into question the results of the studies and trials described in the Prospectus; and the Company has not received any written notice or correspondence from the FDA or any foreign, state or local Governmental Authority exercising comparable authority or any institutional review board or comparable authority requiring the termination, suspension, clinical hold or material modification of any studies or trials.

(v) Market Capitalization. At the time the Registration Statement was or will be originally declared effective, and at the time the Company's most recent Annual Report on

Form 10-K was filed with the Commission, the Company met or will meet the then applicable requirements for the use of Form S-3 under the Securities Act, including, but not limited to, General Instruction I.B.1 of Form S-3. The Company is not a shell company (as defined in Rule 405 under the Securities Act) and has not been a shell company for at least 12 calendar months previously and if it has been a shell company at any time previously, has filed current Form 10 information (as defined in Instruction I.B.6 of Form S-3) with the Commission at least 12 calendar months previously reflecting its status as an entity that is not a shell company.

(w) No Material Defaults. Neither the Company nor any of the Subsidiaries has defaulted on any installment on indebtedness for borrowed money or on any rental on one or more long-term leases, which defaults, individually or in the aggregate, would have a Material Adverse Effect. The Company has not filed a report pursuant to Section 13(a) or 15(d) of the Exchange Act since the filing of its last Annual Report on Form 10-K, indicating that it (i) has failed to pay any dividend or sinking fund installment on preferred stock or (ii) has defaulted on any installment on indebtedness for borrowed money or on any rental on one or more long-term leases, which defaults, individually or in the aggregate, would have a Material Adverse Effect.

(x) Certain Market Activities. Neither the Company, nor any of the Subsidiaries, nor any of their respective directors, officers or controlling persons has taken, directly or indirectly, any action designed, or that has constituted or would reasonably be expected to cause or result in, under the Exchange Act or otherwise, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Placement Shares.

(y) Broker/Dealer Relationships. Neither the Company nor any of the Subsidiaries (i) is required to register as a “broker” or “dealer” in accordance with the provisions of the Exchange Act or (ii) directly or indirectly through one or more intermediaries, controls or is a “person associated with a member” or “associated person of a member” (within the meaning set forth in the FINRA Manual).

(z) No Reliance. The Company has not relied upon the Agent or legal counsel for the Agent for any legal, tax or accounting advice in connection with the offering and sale of the Placement Shares.

(aa) Taxes. The Company and each of its Subsidiaries have filed all federal, state, local and foreign tax returns which have been required to be filed and paid all taxes shown thereon through the date hereof, to the extent that such taxes have become due and are not being contested in good faith, except where the failure to so file or pay would not have a Material Adverse Effect. Except as otherwise disclosed in or contemplated by the Registration Statement or the Prospectus, no tax deficiency has been determined adversely to the Company or any of its Subsidiaries which has had, or would have, individually or in the aggregate, a Material Adverse Effect. The Company has no knowledge of any federal, state or other governmental tax deficiency, penalty or assessment which has been or might be asserted or threatened against it which would have a Material Adverse Effect.

(bb) Title to Real and Personal Property. Except as set forth in the Registration Statement or the Prospectus, the Company and its Subsidiaries have good and marketable title in fee simple to all items of real property owned by them, good and valid title to all tangible

personal property described in the Registration Statement or Prospectus as being owned by them, in each case free and clear of all liens, encumbrances and claims, except those matters that (i) do not materially interfere with the use made and proposed to be made of such property by the Company and any of its Subsidiaries or (ii) would not, individually or in the aggregate, have a Material Adverse Effect. Any real or tangible personal property described in the Registration Statement or Prospectus as being leased by the Company and any of its Subsidiaries is held by them under valid, existing and enforceable leases, except those that (A) do not materially interfere with the use made or proposed to be made of such property by the Company or any of its Subsidiaries or (B) would not be reasonably expected, individually or in the aggregate, to have a Material Adverse Effect. Each of the properties of the Company and its Subsidiaries complies with all applicable codes, laws and regulations (including, without limitation, building and zoning codes, laws and regulations and laws relating to access to such properties), except if and to the extent disclosed in the Registration Statement or Prospectus or except for such failures to comply that would not, individually or in the aggregate, reasonably be expected to interfere in any material respect with the use made and proposed to be made of such property by the Company and its Subsidiaries or otherwise have a Material Adverse Effect. None of the Company or its subsidiaries has received from any Governmental Authorities any notice of any condemnation of, or zoning change affecting, the properties of the Company and its Subsidiaries, and the Company knows of no such condemnation or zoning change which is threatened, except for such that would not reasonably be expected to interfere in any material respect with the use made and proposed to be made of such property by the Company and its Subsidiaries or otherwise have a Material Adverse Effect, individually or in the aggregate.

(cc) Environmental Laws. Except as set forth in the Registration Statement or the Prospectus, the Company and its Subsidiaries (i) are in compliance with any and all applicable federal, state, local and foreign laws, rules, regulations, decisions and orders relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or contaminants (collectively, "**Environmental Laws**"); (ii) have received and are in compliance with all permits, licenses or other approvals required of them under applicable Environmental Laws to conduct their respective businesses as described in the Registration Statement and the Prospectus; and (iii) have not received notice of any actual or potential liability for the investigation or remediation of any disposal or release of hazardous or toxic substances or wastes, pollutants or contaminants, except, in the case of any of clauses (i), (ii) or (iii) above, for any such failure to comply or failure to receive required permits, licenses, other approvals or liability as would not, individually or in the aggregate, have a Material Adverse Effect.

(dd) Disclosure Controls. The Company and each of its Subsidiaries maintain systems of internal accounting controls designed to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles ("GAAP") and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences. The Company's internal control over financial reporting is effective and the Company is not aware of any material weaknesses in its internal control over financial reporting

(other than as set forth in the Prospectus). Since the date of the latest audited financial statements of the Company included in the Prospectus, there has been no change in the Company's internal control over financial reporting that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting (other than as set forth in the Prospectus). The Company has established disclosure controls and procedures (as defined in Exchange Act Rules 13a-15 and 15d-15) for the Company and designed such disclosure controls and procedures to provide reasonable assurance that material information relating to the Company and each of its Subsidiaries is made known to the certifying officers by others within those entities, including during the period in which the Company's Annual Report on Form 10-K or Quarterly Report on Form 10-Q, as the case may be, is being prepared. The Company's certifying officers have evaluated the effectiveness of the Company's disclosure controls and procedures as of a date within 90 days prior to the filing date of the Form 10-K for the fiscal year most recently ended (such date, the **"Evaluation Date**"). The Company presented in its Form 10-K for the fiscal year most recently ended the conclusions of the certifying officers about the effectiveness of the disclosure controls and procedures based on their evaluations as of the Evaluation Date and the disclosure controls and procedures were effective. Since the Evaluation Date, there have been no significant changes in the Company's internal controls (as such term is defined in Item 307(b) of Regulation S-K under the Securities Act) or, to the Company's knowledge, in other factors that could significantly affect the Company's internal controls.

(ee) Sarbanes-Oxley. There is and has been no failure on the part of the Company or any of the Company's directors or officers, in their capacities as such, to comply in all material respects with any applicable provisions of the Sarbanes-Oxley Act and the rules and regulations promulgated thereunder. Each of the principal executive officer and the principal financial officer of the Company (or each former principal executive officer of the Company and each former principal financial officer of the Company as applicable) has made all certifications required by Sections 302 and 906 of the Sarbanes-Oxley Act with respect to all reports, schedules, forms, statements and other documents required to be filed by it or furnished by it to the Commission. For purposes of the preceding sentence, "principal executive officer" and "principal financial officer" shall have the meanings given to such terms in the Sarbanes-Oxley Act.

(ff) Finder's Fees. Neither the Company nor any of the Subsidiaries has incurred any liability for any finder's fees, brokerage commissions or similar payments in connection with the transactions herein contemplated, except as may otherwise exist with respect to Agent pursuant to this Agreement.

(gg) Labor Disputes. No labor disturbance by or dispute with employees of the Company or any of its Subsidiaries exists or, to the knowledge of the Company, is threatened which would result in a Material Adverse Effect.

(hh) Investment Company Act. Neither the Company nor any of the Subsidiaries is or, after giving effect to the offering and sale of the Placement Shares, will be an "investment company" or an entity "controlled" by an "investment company," as such terms are defined in the Investment Company Act of 1940, as amended (the "**Investment Company Act**").

(ii) Operations. The operations of the Company and its Subsidiaries are and have been conducted at all times in compliance with applicable financial record keeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all jurisdictions to which the Company or its Subsidiaries are subject, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any Governmental Authority (collectively, the "**Money Laundering Laws**") and no action, suit or proceeding by or before any Governmental Authority involving the Company or any of its Subsidiaries with respect to the Money Laundering Laws is pending or, to the knowledge of the Company, threatened.

(jj) Off-Balance Sheet Arrangements. There are no transactions, arrangements and other relationships between and/or among the Company and/or, to the knowledge of the Company, any of its affiliates and any unconsolidated entity, including, but not limited to, any structured finance, special purpose or limited purpose entity (each, an "**Off-Balance Sheet Transaction**") that would reasonably be expected to affect materially the Company's liquidity or the availability of or requirements for its capital resources, including those Off-Balance Sheet Transactions described in the Commission's Statement about Management's Discussion and Analysis of Financial Conditions and Results of Operations (Release Nos. 33-8056; 34-45321; FR-61), required to be described in the Prospectus which have not been described as required.

(kk) Underwriter Agreements. The Company is not a party to any agreement with an agent or underwriter for any other "at the market" or continuous equity transaction.

(ll) ERISA. To the knowledge of the Company, each material employee benefit plan, within the meaning of Section 3(3) of the Employee Retirement Income Security Act of 1974, as amended ("**ERISA**"), that is maintained, administered or contributed to by the Company or any of its affiliates for employees or former employees of the Company and any of its Subsidiaries has been maintained in material compliance with its terms and the requirements of any applicable statutes, orders, rules and regulations, including but not limited to ERISA and the Internal Revenue Code of 1986, as amended (the "**Code**"); no prohibited transaction, within the meaning of Section 406 of ERISA or Section 4975 of the Code, has occurred which would result in a material liability to the Company with respect to any such plan excluding transactions effected pursuant to a statutory or administrative exemption; and for each such plan that is subject to the funding rules of Section 412 of the Code or Section 302 of ERISA, no "accumulated funding deficiency" as defined in Section 412 of the Code has been incurred, whether or not waived, and the fair market value of the assets of each such plan (excluding for these purposes accrued but unpaid contributions) exceeds the present value of all benefits accrued under such plan determined using reasonable actuarial assumptions.

(mm) Forward-Looking Statements. No forward-looking statement (within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act) (a "**Forward-Looking Statement**") contained in the Registration Statement and the Prospectus has been made or reaffirmed without a reasonable basis or has been disclosed other than in good faith.

(nn) Agent Purchases. The Company acknowledges and agrees that Agent has informed the Company that the Agent may, to the extent permitted under the Securities Act and

the Exchange Act, purchase and sell Common Stock for its own account while this Agreement is in effect, *provided*, that the Company shall not be deemed to have authorized or consented to any such purchases or sales by the Agent.

(oo) Margin Rules. Neither the issuance, sale and delivery of the Placement Shares nor the application of the proceeds thereof by the Company as described in the Registration Statement and the Prospectus will violate Regulation T, U or X of the Board of Governors of the Federal Reserve System or any other regulation of such Board of Governors.

(pp) Insurance. The Company and each of its Subsidiaries carry, or are covered by, insurance in such amounts and covering such risks as the Company and each of its Subsidiaries reasonably believe are adequate for the conduct of their properties and as is customary for companies engaged in similar businesses in similar industries.

(qq) No Improper Practices. (i) Neither the Company nor the Subsidiaries, nor to the Company's knowledge, any of their respective directors, executive officers, employees, agents, affiliates, or other persons acting on behalf of the Company or any Subsidiary, has, in the past five years, made any unlawful contributions to any candidate for any political office (or failed fully to disclose any contribution in violation of applicable law) or made any contribution or other payment to any official of, or candidate for, any federal, state, municipal, or foreign office or other person charged with similar public or quasi-public duty in violation of any applicable law or of the character required to be disclosed in the Prospectus; (ii) no relationship, direct or indirect, exists between or among the Company or any Subsidiary, or to the Company's knowledge, any affiliate of any of them, on the one hand, and, to the Company's knowledge, the directors, officers and stockholders of the Company or any Subsidiary, on the other hand, that is required by the Securities Act to be described in the Registration Statement and the Prospectus that is not so described; (iii) no relationship, direct or indirect, exists between or among the Company or any Subsidiary or any affiliate of them, on the one hand, and to the Company's knowledge, the directors, officers, or stockholders of the Company or any Subsidiary, on the other hand, that is required by the rules of FINRA to be described in the Registration Statement and the Prospectus that is not so described; (iv) except as described in the Registration Statement and the Prospectus, there are no material outstanding loans or advances or material guarantees of indebtedness by the Company or any Subsidiary to or for the benefit of any of their respective officers or directors or any of the members of the families of any of them; (v) the Company has not offered, or caused any placement agent to offer, Common Stock to any person with the intent to influence unlawfully (A) a customer or supplier of the Company or any Subsidiary to alter the customer's or supplier's level or type of business with the Company or any Subsidiary or (B) a trade journalist or publication to write or publish favorable information about the Company or any Subsidiary or any of their respective products or services, and (vi) neither the Company nor any Subsidiary nor to the Company's knowledge any director, officer, employee, any agent, affiliate, or other person acting on behalf of the Company or any Subsidiary has (A) violated or is in violation of any applicable provision of the U.S. Foreign Corrupt Practices Act of 1977, as amended, or any other applicable anti-bribery or anti-corruption law (collectively, "**Anti-Corruption Laws**"), (B) promised, offered, provided, attempted to provide, or authorized the provision of anything of value, directly or indirectly, to any person for the purpose of obtaining or retaining business, influencing any act or decision of the recipient, or securing any improper advantage; or (C) made any payment of funds of the Company or any Subsidiary or received or retained any funds in violation of any Anti-Corruption Laws.

(rr) Status Under the Securities Act. The Company was not and is not an ineligible issuer as defined in Rule 405 under the Securities Act at the times specified in Rules 164 and 433 under the Securities Act in connection with the offering of the Placement Shares.

(ss) No Misstatement or Omission in an Issuer Free Writing Prospectus. Each Issuer Free Writing Prospectus, as of its issue date and as of each Applicable Time (as defined in Section 23 below), did not, does not and will not, through the completion of the Placement for which such Issuer Free Writing Prospectus is used or deemed used, include any information that conflicted, conflicts or will conflict with the information contained in the Registration Statement or the Prospectus, including any Incorporated Document that has not been superseded or modified. The foregoing sentence does not apply to statements in or omissions from any Issuer Free Writing Prospectus based upon and in conformity with written information furnished to the Company by the Agent specifically for use therein.

(tt) No Conflicts. Neither the execution of this Agreement by the Company, nor the issuance, offering or sale of the Placement Shares, nor the consummation by the Company of any of the transactions contemplated herein, nor the compliance by the Company with the terms and provisions hereof will conflict with, or will result in a breach of, any of the terms and provisions of, or has constituted or will constitute a default under, or has resulted in or will result in the creation or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to the terms of any contract or other agreement to which the Company may be bound or to which any of the property or assets of the Company is subject, except (i) such conflicts, breaches or defaults as may have been waived and (ii) such conflicts, breaches and defaults that would not have a Material Adverse Effect; nor will such action result (x) in any violation of the provisions of the organizational or governing documents of the Company, or (y) in any violation of the provisions of any statute or any order, rule or regulation applicable to the Company or of any Governmental Authority having jurisdiction over the Company, other than, with respect to clause (y), any violation that would not reasonably be expected to have a Material Adverse Effect.

(uu) Sanctions. (i) The Company represents that, neither the Company nor any of its Subsidiaries (collectively, the "**Entity**") or, to such Entity's knowledge, any director, officer, employee, agent, affiliate or representative of the Entity, is a government, individual, or entity (in this paragraph (uu), "**Person**") that is, or is owned or controlled by a Person that is:

(A) the subject of any applicable sanctions administered or enforced by the U.S. Department of Treasury's Office of Foreign Assets Control ("**OFAC**"), the United Nations Security Council, the European Union, Her Majesty's Treasury, or other relevant sanctions authorities, including, without limitation, designation on OFAC's Specially Designated Nationals and Blocked Persons List or OFAC's Foreign Sanctions Evaders List (as amended, collectively, "**Sanctions**"), nor

(B) located, organized or resident in a country or territory that is the subject of Sanctions that broadly prohibit dealings with that country or territory (including, without limitation, Cuba, Iran, North Korea, Sudan, Syria, and the Crimea Region of the Ukraine) (the "**Sanctioned Countries**").

(ii) The Entity represents and covenants that it will not, directly or indirectly, use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any subsidiary, joint venture partner or other Person:

(A) to fund or facilitate any activities or business of or with any Person or in any country or territory that, at the time of such funding or facilitation, is the subject of Sanctions or is a Sanctioned Country; or

(B) in any other manner that will result in a violation of Sanctions by any Person (including any Person participating in the offering, whether as underwriter, advisor, investor or otherwise).

(iii) The Entity represents and covenants that, except as detailed in the Registration Statement and the Prospectus, for the past 5 years, it has not knowingly engaged in, is not now knowingly engaging in, and will not knowingly engage in, any dealings or transactions with any Person, or in any country or territory, that at the time of the dealing or transaction is or was the subject of Sanctions or is or was a Sanctioned Country.

(vv) Stock Transfer Taxes. On each Settlement Date, all stock transfer or other taxes (other than income taxes) which are required to be paid in connection with the sale and transfer of the Placement Shares to be sold hereunder will be, or will have been, fully paid or provided for by the Company and all laws imposing such taxes will be or will have been fully complied with.

(ww) Compliance with Laws. Each of the Company and its Subsidiaries: (A) is and at all times has been in compliance with all statutes or regulations applicable to the ownership, testing, development, manufacture, packaging, processing, use, distribution, marketing, labeling, promotion, sale, offer for sale, storage, import, export or disposal of any product manufactured or distributed by the Company or its Subsidiaries ("**Applicable Laws**"), except as could not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; (B) has not received any FDA Form 483, notice of adverse finding, warning letter, untitled letter or other written correspondence or notice from the FDA or any other Governmental Authority alleging or asserting noncompliance with any Applicable Laws or any licenses, certificates, approvals, clearances, authorizations, permits and supplements or amendments thereto required by any such Applicable Laws ("**Authorizations**"); (C) possesses all material Authorizations and such Authorizations are valid and in full force and effect and are not in material violation of any term of any such Authorizations; (D) has not received written notice of any claim, action, suit, proceeding, hearing, enforcement, investigation, arbitration or other action from any Governmental Authority or third party alleging that any product operation or activity is in violation of any Applicable Laws or Authorizations and has no knowledge that any such Governmental Authority or third party is considering any such claim, litigation, arbitration, action, suit, investigation or proceeding; (E) has not received written notice that any Governmental Authority has taken, is taking or intends to take action to limit, suspend, modify or revoke any Authorizations and has no knowledge that any such Governmental Authority is considering such action; (F) has filed, obtained, maintained or submitted all material reports,

documents, forms, notices, applications, records, claims, submissions and supplements or amendments as required by any Applicable Laws or Authorizations and that all such reports, documents, forms, notices, applications, records, claims, submissions and supplements or amendments were complete and correct on the date filed (or were corrected or supplemented by a subsequent submission), except as would not, individually or in the aggregate, reasonably be expected to result in a Material Adverse Effect; and (G) has not, either voluntarily or involuntarily, initiated, conducted, or issued or caused to be initiated, conducted or issued, any recall, market withdrawal or replacement, safety alert, post sale warning, "dear healthcare provider" letter, or other notice or action relating to the alleged lack of safety or efficacy of any product or any alleged product defect or violation and, to the Company's knowledge, no third party has initiated, conducted or intends to initiate any such notice or action.

(xx) Statistical and Market-Related Data. The statistical, demographic and market-related data included in the Registration Statement and Prospectus are based on or derived from sources that the Company believes to be reliable and accurate or represent the Company's good faith estimates that are made on the basis of data derived from such sources.

(yy) Emerging Growth Company Status. From the time of the initial filing of the Company's Registration Statement on Form S-1 with the Commission through the date hereof, the Company has been and is an "emerging growth company," as defined in Section 2(a) of the Securities Act (an "**Emerging Growth Company**").

Any certificate signed by an officer of the Company and delivered to the Agent or to counsel for the Agent pursuant to or in connection with this Agreement shall be deemed to be a representation and warranty by the Company, as applicable, to the Agent as to the matters set forth therein.

7. Covenants of the Company. The Company covenants and agrees with Agent that:

(a) Registration Statement Amendments. After the date of this Agreement and during any period in which a Prospectus relating to any Placement Shares is required to be delivered by Agent under the Securities Act (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), (i) the Company will notify the Agent promptly of the time when any subsequent amendment to the Registration Statement, other than documents incorporated by reference, has been filed with the Commission and/or has become effective or any subsequent supplement to the Prospectus has been filed and of any request by the Commission for any amendment or supplement to the Registration Statement or Prospectus or for additional information, (ii) the Company will prepare and file with the Commission, promptly upon the Agent's request, any amendments or supplements to the Registration Statement or Prospectus that, in the Agent's reasonable opinion, may be necessary or advisable in connection with the distribution of the Placement Shares by the Agent (*provided*, *however*, that the failure of the Agent to make such request shall not relieve the Company of any obligation or liability hereunder, or affect the Agent's right to rely on the representations and warranties made by the Company in this Agreement and *provided*, *further*, that the only remedy the Agent shall have with respect to the failure to make such filing shall be to cease making sales under this Agreement until such amendment or supplement is filed); (iii) the Company will not file any amendment or supplement to the Registration Statement or Prospectus relating to the Placement Shares or a security convertible into the Placement Shares

unless a copy thereof has been submitted to Agent within a reasonable period of time before the filing and the Agent has not reasonably objected in writing thereto within two (2) Business Day (*provided*, *however*, that the failure of the Agent to make such objection shall not relieve the Company of any obligation or liability hereunder, or affect the Agent's right to rely on the representations and warranties made by the Company in this Agreement and the Company has no obligation to provide the Agent any advance copy of such filing or to provide the Agent any opportunity to object to such filing if such filing does not name the Agent and does not relate to the transactions contemplated by this Agreement, and *provided*, *further*, that the only remedy the Agent shall have with respect to the failure by the Company to seek such consent shall be to cease making sales under this Agreement) and the Company will furnish to the Agent at the time of filing thereof a copy of any document that upon filing is deemed to be incorporated by reference into the Registration Statement or Prospectus, except for those documents available via EDGAR; and (iv) the Company will cause each amendment or supplement to the Prospectus to be filed with the Commission as required pursuant to the applicable paragraph of Rule 424(b) of the Securities Act or, in the case of any document to be incorporated therein by reference, to be filed with the Commission as required pursuant to the Exchange Act, within the time period prescribed (the determination to file or not file any amendment or supplement with the Commission under this Section 7(a), based on the Company's reasonable opinion or reasonable objections, shall be made exclusively by the Company).

(b) Notice of Commission Stop Orders. The Company will advise the Agent, promptly after it receives notice or obtains knowledge thereof, of the issuance or threatened issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement, of the suspension of the qualification of the Placement Shares for offering or sale in any jurisdiction, or of the initiation or threatening of any proceeding for any such purpose; and it will promptly use its commercially reasonable efforts to prevent the issuance of any stop order or to obtain its withdrawal if such a stop order should be issued. The Company will advise the Agent promptly after it receives any request by the Commission for any amendments to the Registration Statement or any amendment or supplements to the Prospectus or any Issuer Free Writing Prospectus or for additional information related to the offering of the Placement Shares or for additional information related to the Registration Statement, the Prospectus or any Issuer Free Writing Prospectus.

(c) Delivery of Prospectus; Subsequent Changes. During any period in which a Prospectus relating to the Placement Shares is required to be delivered by the Agent under the Securities Act with respect to the offer and sale of the Placement Shares, (including in circumstances where such requirement may be satisfied pursuant to Rule 172 under the Securities Act or similar rule), the Company will comply with all requirements imposed upon it by the Securities Act, as from time to time in force, and to file on or before their respective due dates all reports and any definitive proxy or information statements required to be filed by the Company with the Commission pursuant to Sections 13(a), 13(c), 14, 15(d) or any other provision of or under the Exchange Act. If the Company has omitted any information from the Registration Statement pursuant to Rule 430B under the Securities Act, it will use its best efforts to comply with the provisions of and make all requisite filings with the Commission pursuant to said Rule 430B and to notify the Agent promptly of all such filings. If during such period any event occurs as a result of which the Prospectus as then amended or supplemented would include an untrue statement of a material fact or omit to state a material fact necessary to make the

statements therein, in the light of the circumstances then existing, not misleading, or if during such period it is necessary to amend or supplement the Registration Statement or Prospectus to comply with the Securities Act, the Company will promptly notify the Agent to suspend the offering of Placement Shares during such period and the Company will promptly amend or supplement the Registration Statement or Prospectus (at the expense of the Company) so as to correct such statement or omission or effect such compliance; provided, however, that the Company may delay any such amendment or supplement if, in the reasonable judgement of the Company, it is in the best interest of the Company to do so.

(d) Listing of Placement Shares. Prior to the date of the first Placement Notice, the Company will use its reasonable best efforts to cause the Placement Shares to be listed on the Exchange.

(e) Delivery of Registration Statement and Prospectus. The Company will furnish to the Agent and its counsel (at the expense of the Company) copies of the Registration Statement, the Prospectus (including all Incorporated Documents) and all amendments and supplements to the Registration Statement or Prospectus that are filed with the Commission during any period in which a Prospectus relating to the Placement Shares is required to be delivered under the Securities Act (including all Incorporated Documents filed with the Commission during such period), in each case as soon as reasonably practicable and in such quantities as the Agent may from time to time reasonably request and, at the Agent's request, will also furnish copies of the Prospectus to each exchange or market on which sales of the Placement Shares may be made; *provided*, *however*, that the Company shall not be required to furnish any document (other than the Prospectus) to the Agent to the extent such document is available on EDGAR.

(f) Earning Statement. To the extent not available on EDGAR, the Company will make generally available to its security holders as soon as practicable, but in any event not later than 15 months after the end of the Company's current fiscal quarter, an earnings statement covering a 12-month period that satisfies the provisions of Section 11(a) and Rule 158 of the Securities Act.

(g) Use of Proceeds. The Company will use the Net Proceeds as described in the Prospectus in the section entitled "Use of Proceeds."

(h) Notice of Other Sales. Without the prior written consent of the Agent, the Company will not, directly or indirectly, offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Common Stock (other than the Placement Shares offered pursuant to this Agreement) or securities convertible into or exchangeable for Common Stock, warrants or any rights to purchase or acquire, Common Stock during the period beginning on the fifth (5th) Trading Day immediately prior to the date on which any Placement Notice is delivered to Agent hereunder and ending on the fifth (5th) Trading Day immediately following the final Settlement Date with respect to Placement Shares sold pursuant to such Placement Notice (or, if the Placement Notice has been terminated or suspended prior to the sale of all Placement Shares covered by a Placement Notice, the date of such suspension or termination); and will not directly or indirectly in any other "at the market" or continuous equity transaction offer to sell, sell, contract to sell, grant any option to sell or otherwise dispose of any Common Stock (other than the Placement Shares offered pursuant to this Agreement) or securities convertible into or

exchangeable for Common Stock, warrants or any rights to purchase or acquire, Common Stock prior to the later of the termination of this Agreement and the sixtieth (60th) day immediately following the final Settlement Date with respect to Placement Shares sold pursuant to such Placement Notice; *provided*, *however*, that such restrictions will not apply in connection with the Company's issuance or sale of (i) Common Stock, options to purchase Common Stock, restricted stock or restricted stock units or other equity awards to acquire Common Stock, or Common Stock issuable upon the exercise of options or settlement of restricted stock units or other equity awards, pursuant to any equity incentive or benefits plan, stock ownership plan, employee stock purchase plan or dividend reinvestment plan (but not Common Stock subject to a waiver to exceed plan limits in its dividend reinvestment plan) of the Company whether now in effect or hereafter implemented, (ii) Common Stock issuable upon conversion of securities or the exercise or vesting of warrants, options or other rights in effect or outstanding, and disclosed in filings by the Company available on EDGAR or otherwise in writing to the Agent and (iii) Common Stock or securities convertible into or exchangeable for shares of Common Stock as consideration for mergers, acquisitions, other business combinations or strategic alliances, or offered and sold in privately negotiated transactions with vendors, customers, consultants, lenders, or strategic partners, occurring after the date of this Agreement which are not issued for capital raising purposes(other than options or other equity issued in connection with a debt facility whereby issuance is not the primary purpose of the debt) and conducted in a manner so as not to be integrated with the offering of Placement Shares hereby.

(i) Change of Circumstances. The Company will, at any time during the pendency of a Placement Notice advise the Agent promptly after it shall have received notice or obtained knowledge thereof, of any information or fact that would alter or affect in any material respect any opinion, certificate, letter or other document required to be provided to the Agent pursuant to this Agreement.

(j) Due Diligence Cooperation. The Company will cooperate with any reasonable due diligence review conducted by the Agent or its representatives in connection with the transactions contemplated hereby, including, without limitation, providing information and making available documents and senior corporate officers, during regular business hours and at the Company's principal offices, as the Agent may reasonably request.

(k) Required Filings Relating to Placement of Placement Shares. To the extent that the filing of a prospectus supplement with the Commission with respect to the placement of the Placement Shares becomes required under Rule 424(b) under the Securities Act, the Company agrees that on such dates as the Securities Act shall require, the Company will (i) file a prospectus supplement with the Commission under the applicable paragraph of Rule 424(b) under the Securities Act (each and every filing date under Rule 424(b), a "**Filing Date**"), which prospectus supplement will set forth, within the relevant period, the amount of Placement Shares sold through the Agent, the Net Proceeds to the Company and the compensation payable by the Company to the Agent with respect to such Placement Shares, and (ii) deliver such number of copies of each such prospectus supplement to each exchange or market on which such sales were effected as may be required by the rules or regulations of such exchange or market.

(l) Representation Dates; Certificate. (1) On or prior to the date of the first Placement Notice and (2) following the delivery of the first Placement Notice each time during the term of this Agreement the Company:

(i) files the Prospectus relating to the Placement Shares or amends or supplements (other than a prospectus supplement relating solely to an offering of securities other than the Placement Shares) the Registration Statement or the Prospectus relating to the Placement Shares by means of a post-effective amendment, sticker, or supplement but not by means of incorporation of documents by reference into the Registration Statement or the Prospectus relating to the Placement Shares;

(ii) files an annual report on Form 10-K under the Exchange Act (including any Form 10-K/A containing amended financial information or a material amendment to the previously filed Form 10-K);

(iii) files its quarterly reports on Form 10-Q under the Exchange Act; or

(iv) files a current report on Form 8-K containing amended financial information (other than information "furnished" pursuant to Items 2.02 or 7.01 of Form 8-K or to provide disclosure pursuant to Item 8.01 of Form 8-K relating to the reclassification of certain properties as discontinued operations in accordance with Statement of Financial Accounting Standards No. 144) under the Exchange Act (each date of filing of one or more of the documents referred to in clauses (i) through (iv) shall be a "**Representation Date**");

the Company shall furnish the Agent (but in the case of clause (iv) above only if the Agent reasonably determines that the information contained in such Form 8-K is material) with a certificate dated the Representation Date, in the form and substance satisfactory to the Agent and its counsel, substantially similar to the form previously provided to the Agent and its counsel, modified, as necessary, to relate to the Registration Statement and the Prospectus as amended or supplemented. The requirement to provide a certificate under this Section 7(l) shall be automatically waived for any Representation Date occurring (1) at a time a Suspension is in effect, which waiver shall continue until the earlier to occur of the date the Company delivers instructions for the sale of Placement Shares hereunder (which for such calendar quarter shall be considered a Representation Date) and the next occurring Representation Date, and (2) at a time at which no Placement Notice is pending hereunder, which waiver shall continue until the date the Company delivers a Placement Notice hereunder (which for such calendar quarter shall be considered a Representation Date). Notwithstanding the foregoing, if the Company subsequently decides to sell Placement Shares following a Representation Date when the Company relied on such waiver and did not provide the Agent with a certificate under this Section 7(l), then before the Company delivers the instructions for the sale of Placement Shares or the Agent sells any Placement Shares pursuant to such instructions, the Company shall provide the Agent with a certificate in conformity with this Section 7(l) dated as of the date that the instructions for the sale of Placement Shares are issued.

(m) Legal Opinion. (1) On or prior to the date of the first Placement Notice and (2) unless waived by the Agent, within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable (including, for the avoidance of doubt, any automatic waiver pursuant to Section 7(l)) and excluding the date of this Agreement, the Company shall cause to be furnished to the Agent a written opinion of Goodwin Procter LLP ("**Company Counsel**"), or other counsel satisfactory to the Agent, in form and substance satisfactory to Agent and its

counsel; *provided*, *however*, the Company shall be required to furnish to Agent no more than one opinion hereunder per calendar quarter and the Company shall not be required to furnish any such letter if the Company does not intend to deliver a Placement Notice in such calendar quarter until such time as the Company delivers its next Placement Notice; *provided*, *further*, that in lieu of such opinions for subsequent periodic filings under the Exchange Act, counsel may furnish the Agent with a letter (a "**Reliance Letter**") to the effect that the Agent may rely on a prior opinion delivered under this Section 7(m) to the same extent as if it were dated the date of such letter (except that statements in such prior opinion shall be deemed to relate to the Registration Statement and the Prospectus as amended or supplemented as of the date of the Reliance Letter).

(n) Comfort Letter. (1) On or prior to the date of the first Placement Notice and (2) unless waived by the Agent, within five (5) Trading Days of each Representation Date with respect to which the Company is obligated to deliver a certificate pursuant to Section 7(l) for which no waiver is applicable (including, for the avoidance of doubt, any automatic waiver pursuant to Section 7(l)) and excluding the date of this Agreement, the Company shall cause its independent registered public accounting firm to furnish the Agent letters (the "**Comfort Letters**"), dated the date the Comfort Letter is delivered, which shall meet the requirements set forth in this Section 7(n); *provided*, that if requested by the Agent, the Company shall cause a Comfort Letter to be furnished to the Agent within ten (10) Trading Days of the date of occurrence of any material transaction or event requiring the filing of a Current Report on Form 8-K containing material financial information (including the restatement of the Company's financial statements). The Comfort Letter from the Company's independent registered public accounting firm shall be in a form and substance reasonably satisfactory to the Agent, (i) confirming that they are an independent registered public accounting firm within the meaning of the Securities Act and the PCAOB, (ii) stating, as of such date, the conclusions and findings of such firm with respect to the financial information and other matters ordinarily covered by accountants' "comfort letters" to underwriters in connection with registered public offerings (the first such letter, the "**Initial Comfort Letter**") and (iii) updating the Initial Comfort Letter with any information that would have been included in the Initial Comfort Letter had it been given on such date and modified as necessary to relate to the Registration Statement and the Prospectus, as amended and supplemented to the date of such letter.

(o) Market Activities. The Company will not, directly or indirectly, (i) take any action designed to cause or result in, or that constitutes or would reasonably be expected to constitute, the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of Common Stock or (ii) sell, bid for, or purchase Common Stock in violation of Regulation M, or pay anyone any compensation for soliciting purchases of the Placement Shares other than the Agent.

(p) Investment Company Act. The Company will conduct its affairs in such a manner so as to reasonably ensure that neither it nor any of its Subsidiaries will be or become, at any time prior to the termination of this Agreement, required to register as an "investment company," as such term is defined in the Investment Company Act.

(q) No Offer to Sell. Other than an Issuer Free Writing Prospectus approved in advance by the Company and the Agent in its capacity as agent hereunder, neither the Agent nor the Company (including its agents and representatives, other than the Agent in its capacity as such) will make, use, prepare, authorize, approve or refer to any written communication (as defined in Rule 405 under the Securities Act), required to be filed with the Commission, that constitutes an offer to sell or solicitation of an offer to buy Placement Shares hereunder.

(r) Blue Sky and Other Qualifications. The Company will use its commercially reasonable efforts, in cooperation with the Agent, to qualify the Placement Shares for offering and sale, or to obtain an exemption for the Placement Shares to be offered and sold, under the applicable securities laws of such states and other jurisdictions (domestic or foreign) as the Agent may designate and to maintain such qualifications and exemptions in effect for so long as required for the distribution of the Placement Shares (but in no event for less than one year from the date of this Agreement); *provided*, *however*, that the Company shall not be obligated to file any general consent to service of process or to qualify as a foreign corporation or as a dealer in securities in any jurisdiction in which it is not so qualified or to subject itself to taxation in respect of doing business in any jurisdiction in which it is not otherwise so subject. In each jurisdiction in which the Placement Shares have been so qualified or exempt, the Company will file such statements and reports as may be required by the laws of such jurisdiction to continue such qualification or exemption, as the case may be, in effect for so long as required for the distribution of the Placement Shares (but in no event for less than one year from the date of this Agreement).

(s) Sarbanes-Oxley Act. The Company and the Subsidiaries will maintain and keep accurate books and records reflecting their assets and maintain internal accounting controls in a manner designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP and including those policies and procedures that (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company, (ii) provide reasonable assurance that transactions are recorded as necessary to permit the preparation of the Company's consolidated financial statements in accordance with GAAP, (iii) that receipts and expenditures of the Company are being made only in accordance with management's and the Company's directors' authorization, and (iv) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on its financial statements. The Company and the Subsidiaries will maintain such controls and other procedures, including, without limitation, those required by Sections 302 and 906 of the Sarbanes-Oxley Act, and the applicable regulations thereunder that are designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the Commission's rules and forms, including, without limitation, controls and procedures designed to ensure that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive officer and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure and to ensure that material information relating to the Company or the Subsidiaries is made known to them by others within those entities, particularly during the period in which such periodic reports are being prepared.

(t) Secretary's Certificate; Further Documentation. On or prior to the date of the first Placement Notice, the Company shall deliver to the Agent a certificate of the Secretary

of the Company and attested to by an executive officer of the Company, dated as of such date, certifying as to (i) the Certificate of Incorporation of the Company, (ii) the By-laws of the Company, (iii) the resolutions of the Board of Directors of the Company or a duly authorized committee of the Board of Directors of the Company authorizing the execution, delivery and performance of this Agreement and the issuance of the Placement Shares and (iv) the incumbency of the officers duly authorized to execute this Agreement and the other documents contemplated by this Agreement. Within five (5) Trading Days of each Representation Date, the Company shall have furnished to the Agent such further information, certificates and documents as the Agent may reasonably request.

(u) Emerging Growth Company Status. The Company will promptly notify the Agent if the Company ceases to be an Emerging Growth Company at any time during the term of this Agreement.

8. Payment of Expenses. The Company will pay all expenses incident to the performance of its obligations under this Agreement, including (i) the preparation and filing of the Registration Statement, including any fees required by the Commission, and the printing or electronic delivery of the Prospectus as originally filed and of each amendment and supplement thereto, in such number as the Agent shall reasonably deem necessary, (ii) the printing and delivery to the Agent of this Agreement and such other documents as may be required in connection with the offering, purchase, sale, issuance or delivery of the Placement Shares, (iii) the preparation, issuance and delivery of the certificates, if any, for the Placement Shares to the Agent, including any stock or other transfer taxes and any capital duties, stamp duties or other duties or taxes payable upon the sale, issuance or delivery of the Placement Shares to the Agent, (iv) the reasonable fees and expenses of the Company, including but not limited to the reasonable fees and expenses of the counsel, accountants and other advisors to the Company, (v) the reasonable fees and expenses of Agent including but not limited to the reasonable fees and expenses of the counsel to the Agent, payable upon the execution of this Agreement, in an amount not to exceed $50,000, (vi) the qualification or exemption of the Placement Shares under state securities laws in accordance with the provisions of Section 7(r) hereof, including filing fees, but excluding fees of the Agent's counsel, (vii) the printing and delivery to the Agent of copies of any Permitted Issuer Free Writing Prospectus and the Prospectus and any amendments or supplements thereto in such number as the Agent shall reasonably deem necessary, (viii) the preparation, printing and delivery to the Agent of copies of the blue sky survey, (ix) the fees and expenses of the transfer agent and registrar for the Common Stock, (x) the filing and other fees incident to any review by FINRA of the terms of the sale of the Placement Shares including the fees of the Agent's counsel (subject to the cap, set forth in clause (v) above), and (xi) the fees and expenses incurred in connection with the listing of the Placement Shares on the Exchange.

9. Representations and Covenants of the Agent. The Agent represents and warrants that it is duly registered as a broker-dealer under FINRA, the Exchange Act and the applicable statutes and regulations of each state in which the Placement Shares will be offered and sold, except such states in which the Agent is exempt from registration or such registration is not otherwise required. The Agent shall continue, for the term of this Agreement, to be duly registered as a broker-dealer under FINRA, the Exchange Act and the applicable statutes and regulations of each state in which the Placement Shares will be offered and sold, except such states in which the Agent is exempt from registration or such registration is not otherwise

required, during the term of this Agreement. The Agent will comply in all material respects with all applicable law and regulations in connection with the Placement Shares, including but not limited to Regulation M.

10. Conditions to Agent's Obligations. The obligations of the Agent hereunder with respect to a Placement will be subject to the continuing accuracy and completeness of the representations and warranties made by the Company herein, to the due performance by the Company of its obligations hereunder, to the completion by the Agent of a due diligence review satisfactory to it in its reasonable judgment, and to the continuing satisfaction (or waiver by the Agent in its sole discretion) of the following additional conditions:

(a) Registration Statement Effective. The Registration Statement shall have become effective and shall be available for the (i) resale of all Placement Shares issued to the Agent and not yet sold by the Agent and (ii) sale of all Placement Shares contemplated to be issued by any Placement Notice.

(b) No Material Notices. None of the following events shall have occurred and be continuing: (i) receipt by the Company of any request for additional information from the Commission or any other federal or state Governmental Authority during the period of effectiveness of the Registration Statement, the response to which would require any post-effective amendments or supplements to the Registration Statement or the Prospectus if such post-effective amendments or supplements have not been made or become effective; (ii) the issuance by the Commission or any other federal or state Governmental Authority of any stop order suspending the effectiveness of the Registration Statement or the initiation of any proceedings for that purpose; (iii) receipt by the Company of any notification with respect to the suspension of the qualification or exemption from qualification of any of the Placement Shares for sale in any jurisdiction or the initiation or threatening of any proceeding for such purpose; or (iv) the occurrence of any event that makes any statement of a material fact made in the Registration Statement or the Prospectus or any document incorporated or deemed to be incorporated therein by reference untrue or that requires the making of any changes in the Registration Statement, the Prospectus or documents so that, in the case of the Registration Statement, it will not contain an untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary to make the statements therein not misleading and, that in the case of the Prospectus, it will not contain an untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

(c) No Misstatement or Material Omission. Agent shall not have advised the Company that the Registration Statement or Prospectus, or any amendment or supplement thereto, contains an untrue statement of fact that in the Agent's reasonable opinion is material, or omits to state a fact that in the Agent's reasonable opinion is material and is required to be stated therein or is necessary to make the statements therein not misleading.

(d) Material Changes. Except as contemplated in the Prospectus, or disclosed in the Company's reports filed with the Commission, there shall not have been any material adverse change in the authorized capital stock of the Company or any Material Adverse Effect or any development that would reasonably be expected to cause a Material Adverse Effect, or a downgrading in or withdrawal of the rating assigned to any of the Company's securities (other

than asset backed securities) by any rating organization or a public announcement by any rating organization that it has under surveillance or review its rating of any of the Company's securities (other than asset backed securities), the effect of which, in the case of any such action by a rating organization described above, in the reasonable judgment of the Agent (without relieving the Company of any obligation or liability it may otherwise have), is so material as to make it impracticable or inadvisable to proceed with the offering of the Placement Shares on the terms and in the manner contemplated in the Prospectus.

(e) Legal Opinions. The Agent shall have received the opinions of Company Counsel required to be delivered pursuant to Section 7(m) on or before the date on which such delivery of such opinions is required pursuant to Section 7(m).

(f) Comfort Letter. The Agent shall have received the Comfort Letter required to be delivered pursuant to Section 7(n) on or before the date on which such delivery of such Comfort Letter is required pursuant to Section 7(n).

(g) Representation Certificate. The Agent shall have received the certificate required to be delivered pursuant to Section 7(l) on or before the date on which delivery of such certificate is required pursuant to Section 7(l).

(h) No Suspension. Trading in the Common Stock shall not have been suspended on the Exchange and the Common Stock shall not have been delisted from the Exchange.

(i) Other Materials. On each date on which the Company is required to deliver a certificate pursuant to Section 7(l), the Company shall have furnished to the Agent such appropriate further information, opinions, certificates, letters and other documents as the Agent may reasonably request and which are customarily furnished by an issuer of securities in connection with a securities offering. All such opinions, certificates, letters and other documents will be in compliance with the provisions hereof.

(j) Securities Act Filings Made. All filings with the Commission with respect to the Placement Shares required by Rule 424 under the Securities Act to have been filed prior to the issuance of any Placement Notice hereunder shall have been made within the applicable time period prescribed for such filing by Rule 424.

(k) Approval for Listing. The Placement Shares shall either have been (i) approved for listing on the Exchange, subject only to notice of issuance, or (ii) the Company shall have filed an application for listing of the Placement Shares on the Exchange at, or prior to, the issuance of any Placement Notice, if required, and the Exchange shall have reviewed such application and not provided any objections thereto.

(l) FINRA. If applicable, FINRA shall have raised no objection to the terms of this offering and the amount of compensation allowable or payable to the Agent as described in the Prospectus.

(m) No Termination Event. There shall not have occurred any event that would permit the Agent to terminate this Agreement pursuant to Section 13(a).

11. Indemnification and Contribution.

(a) Company Indemnification. The Company agrees to indemnify and hold harmless the Agent, its affiliates and their respective partners, members, directors, officers, employees and agents and each person, if any, who controls the Agent or any affiliate within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act as follows:

(i) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, joint or several, arising out of or based upon any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement (or any amendment thereto), or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading, or arising out of any untrue statement or alleged untrue statement of a material fact included in any related Issuer Free Writing Prospectus or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading;

(ii) against any and all loss, liability, claim, damage and expense whatsoever, as incurred, joint or several, to the extent of the aggregate amount paid in settlement of any litigation, or any investigation or proceeding by any Governmental Authority, commenced or threatened, or of any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission; *provided* that (subject to Section 10(d) below) any such settlement is effected with the written consent of the Company, which consent shall not unreasonably be delayed or withheld; and

(iii) against any and all expense whatsoever, as incurred (including the fees and disbursements of counsel), reasonably incurred in investigating, preparing or defending against any litigation, or any investigation or proceeding by any Governmental Authority, commenced or threatened, or any claim whatsoever based upon any such untrue statement or omission, or any such alleged untrue statement or omission (whether or not a party), to the extent that any such expense is not paid under (i) or (ii) above,

provided, *however*, that this indemnity agreement shall not apply to any loss, liability, claim, damage or expense to the extent arising out of any untrue statement or omission or alleged untrue statement or omission made solely in reliance upon and in conformity with the Agent Information (as defined below).

(b) Agent Indemnification. Agent agrees to indemnify and hold harmless the Company and its directors and each officer of the Company who signed the Registration Statement, and each person, if any, who controls the Company within the meaning of Section 15 of the Securities Act or Section 20 of the Exchange Act against any and all loss, liability, claim, damage and expense described in the indemnity contained in Section 11(a), as incurred, but only with respect to untrue statements or omissions, or alleged untrue statements or omissions, made in the Registration Statement (or any amendments thereto), the Prospectus (or any amendment or supplement thereto) or any Issuer Free Writing Prospectus (or any amendment or supplement thereto) in reliance upon and in conformity with information relating to the Agent and furnished to the Company in writing by the Agent expressly for use therein. The Company hereby acknowledges that the only information that the Agent has furnished to the Company expressly

for use in the Registration Statement, the Prospectus or any Issuer Free Writing Prospectus (or any amendment or supplement thereto) are the statements set forth in the seventh and eighth paragraphs under the caption "Plan of Distribution" in the Prospectus (the "**Agent Information**").

(c) Procedure. Any party that proposes to assert the right to be indemnified under this Section 11 will, promptly after receipt of notice of commencement of any action against such party in respect of which a claim is to be made against an indemnifying party or parties under this Section 11, notify each such indemnifying party of the commencement of such action, enclosing a copy of all papers served, but the omission so to notify such indemnifying party will not relieve the indemnifying party from (i) any liability that it might have to any indemnified party otherwise than under this Section 11 and (ii) any liability that it may have to any indemnified party under the foregoing provision of this Section 11 unless, and only to the extent that, such omission results in the forfeiture of substantive rights or defenses by the indemnifying party. If any such action is brought against any indemnified party and it notifies the indemnifying party of its commencement, the indemnifying party will be entitled to participate in and, to the extent that it elects by delivering written notice to the indemnified party promptly after receiving notice of the commencement of the action from the indemnified party, jointly with any other indemnifying party similarly notified, to assume the defense of the action, with counsel reasonably satisfactory to the indemnified party, and after notice from the indemnifying party to the indemnified party of its election to assume the defense, the indemnifying party will not be liable to the indemnified party for any legal or other expenses except as provided below and except for the reasonable costs of investigation subsequently incurred by the indemnified party in connection with the defense. The indemnified party will have the right to employ its own counsel in any such action, but the fees, expenses and other charges of such counsel will be at the expense of such indemnified party unless (1) the employment of counsel by the indemnified party has been authorized in writing by the indemnifying party, (2) the indemnified party has reasonably concluded (based on advice of counsel) that there may be legal defenses available to it or other indemnified parties that are different from or in addition to those available to the indemnifying party, (3) a conflict or potential conflict exists (based on advice of counsel to the indemnified party) between the indemnified party and the indemnifying party (in which case the indemnifying party will not have the right to direct the defense of such action on behalf of the indemnified party) or (4) the indemnifying party has not in fact employed counsel to assume the defense of such action or counsel reasonably satisfactory to the indemnified party, in each case, within a reasonable time after receiving notice of the commencement of the action; in each of which cases the reasonable fees, disbursements and other charges of counsel will be at the expense of the indemnifying party or parties. It is understood that the indemnifying party or parties shall not, in connection with any proceeding or related proceedings in the same jurisdiction, be liable for the reasonable fees, disbursements and other charges of more than one separate firm (plus local counsel) admitted to practice in such jurisdiction at any one time for all such indemnified party or parties. All such fees, disbursements and other charges will be reimbursed by the indemnifying party promptly as they are incurred. An indemnifying party will not, in any event, be liable for any settlement of any action or claim effected without its written consent. No indemnifying party shall, without the prior written consent of each indemnified party, settle or compromise or consent to the entry of any judgment in any pending or threatened claim, action or proceeding relating to the matters contemplated by this Section 11 (whether or not any indemnified party is a party thereto), unless

such settlement, compromise or consent (1) includes an express and unconditional release of each indemnified party, in form and substance reasonably satisfactory to such indemnified party, from all liability arising out of such litigation, investigation, proceeding or claim and (2) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(d) Settlement Without Consent if Failure to Reimburse. If an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for reasonable fees and expenses of counsel, such indemnifying party agrees that it shall be liable for any settlement of the nature contemplated by Section 10(a)(ii) effected without its written consent if (1) such settlement is entered into more than 45 days after receipt by such indemnifying party of the aforesaid request, (2) such indemnifying party shall have received notice of the terms of such settlement at least 30 days prior to such settlement being entered into and (3) such indemnifying party shall not have reimbursed such indemnified party in accordance with such request prior to the date of such settlement.

(e) Contribution. In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in the foregoing paragraphs of this Section 10 is applicable in accordance with its terms but for any reason is held to be unavailable or insufficient from the Company or the Agent, the Company and the Agent will contribute to the total losses, claims, liabilities, expenses and damages (including any investigative, legal and other expenses reasonably incurred in connection with, and any amount paid in settlement of, any action, suit or proceeding or any claim asserted) to which the Company and the Agent may be subject in such proportion as shall be appropriate to reflect the relative benefits received by the Company on the one hand and the Agent on the other hand. The relative benefits received by the Company on the one hand and the Agent on the other hand shall be deemed to be in the same proportion as the total net proceeds from the sale of the Placement Shares (before deducting expenses) received by the Company bear to the total compensation received by the Agent from the sale of Placement Shares on behalf of the Company. If, but only if, the allocation provided by the foregoing sentence is not permitted by applicable law, the allocation of contribution shall be made in such proportion as is appropriate to reflect not only the relative benefits referred to in the foregoing sentence but also the relative fault of the Company, on the one hand, and the Agent, on the other hand, with respect to the statements or omission that resulted in such loss, claim, liability, expense or damage, or action in respect thereof, as well as any other relevant equitable considerations with respect to such offering. Such relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or omission or alleged omission to state a material fact relates to information supplied by the Company or the Agent, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Agent agree that it would not be just and equitable if contributions pursuant to this Section 11(e) were to be determined by pro rata allocation or by any other method of allocation that does not take into account the equitable considerations referred to herein. The amount paid or payable by an indemnified party as a result of the loss, claim, liability, expense, or damage, or action in respect thereof, referred to above in this Section 11(e) shall be deemed to include, for the purpose of this Section 11(e), any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim to the extent consistent with Section 11(c) hereof. Notwithstanding the foregoing provisions of this

Section 11(e), the Agent shall not be required to contribute any amount in excess of the commissions received by it under this Agreement and no person found guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) will be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 11(e), any person who controls a party to this Agreement within the meaning of the Securities Act, any affiliates of the Agent and any officers, directors, partners, employees or agents of the Agent or any of its affilaites, will have the same rights to contribution as that party, and each director of the Company and each officer of the Company who signed the Registration Statement will have the same rights to contribution as the Company, subject in each case to the provisions hereof. Any party entitled to contribution, promptly after receipt of notice of commencement of any action against such party in respect of which a claim for contribution may be made under this Section 11(e), will notify any such party or parties from whom contribution may be sought, but the omission to so notify will not relieve that party or parties from whom contribution may be sought from any other obligation it or they may have under this Section 11(e) except to the extent that the failure to so notify such other party materially prejudiced the substantive rights or defenses of the party from whom contribution is sought. Except for a settlement entered into pursuant to the last sentence of Section 11(c) hereof, no party will be liable for contribution with respect to any action or claim settled without its written consent if such consent is required pursuant to Section 11(c) hereof.

12. Representations and Agreements to Survive Delivery. The indemnity and contribution agreements contained in Section 11 of this Agreement and all representations and warranties of the Company herein or in certificates delivered pursuant hereto shall survive, as of their respective dates, regardless of (i) any investigation made by or on behalf of the Agent, any controlling persons, or the Company (or any of their respective officers, directors, employees or controlling persons), (ii) delivery and acceptance of the Placement Shares and payment therefor or (iii) any termination of this Agreement.

13. Termination.

(a) The Agent may terminate this Agreement, by notice to the Company, as hereinafter specified at any time (1) if there has been, since the time of execution of this Agreement or since the date as of which information is given in the Prospectus, any change, or any development or event involving a prospective change, in the condition, financial or otherwise, or in the business, properties, earnings, results of operations or prospects of the Company and its Subsidiaries considered as one enterprise, whether or not arising in the ordinary course of business, which individually or in the aggregate, in the sole judgment of the Agent is material and adverse and makes it impractical or inadvisable to market the Placement Shares or to enforce contracts for the sale of the Placement Shares, (2) if there has occurred any material adverse change in the financial markets in the United States or the international financial markets, any outbreak of hostilities or escalation thereof or other calamity or crisis or any change or development involving a prospective change in national or international political, financial or economic conditions, in each case the effect of which is such as to make it, in the judgment of the Agent, impracticable or inadvisable to market the Placement Shares or to enforce contracts for the sale of the Placement Shares, (3) if trading in the Common Stock has been suspended or limited by the Commission or the Exchange, or if trading generally on the Exchange has been suspended or limited, or minimum prices for trading have been fixed on the Exchange, (4) if any

suspension of trading of any securities of the Company on any exchange or in the over-the-counter market shall have occurred and be continuing, (5) if a major disruption of securities settlements or clearance services in the United States shall have occurred and be continuing, or (6) if a banking moratorium has been declared by either U.S. Federal or New York authorities. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8 (Payment of Expenses), Section 11 (Indemnification and Contribution), Section 12 (Representations and Agreements to Survive Delivery), Section 18 (Governing Law and Time; Waiver of Jury Trial) and Section 19 (Consent to Jurisdiction) hereof shall remain in full force and effect notwithstanding such termination. If the Agent elects to terminate this Agreement as provided in this Section 13(a), the Agent shall provide the required notice as specified in Section 14 (Notices).

(b) The Company shall have the right, by giving ten (10) days' notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8, Section 11, Section 17, Section 18 and Section 19 hereof shall remain in full force and effect notwithstanding such termination.

(c) The Agent shall have the right, by giving ten (10) days notice as hereinafter specified to terminate this Agreement in its sole discretion at any time after the date of this Agreement. Any such termination shall be without liability of any party to any other party except that the provisions of Section 8, Section 11, Section 17, Section 18 and Section 19 hereof shall remain in full force and effect notwithstanding such termination.

(d) This Agreement shall remain in full force and effect unless terminated pursuant to Sections 13(a), (b), or (c) above or otherwise by mutual agreement of the parties; *provided*, *however*, that any such termination by mutual agreement shall in all cases be deemed to provide that Section 8, Section 11, Section 17, Section 18 and Section 19 shall remain in full force and effect.

(e) Any termination of this Agreement shall be effective on the date specified in such notice of termination; *provided*, *however*, that such termination shall not be effective until the close of business on the date of receipt of such notice by the Agent or the Company, as the case may be. If such termination shall occur prior to the Settlement Date for any sale of Placement Shares, such Placement Shares shall settle in accordance with the provisions of this Agreement.

14. Notices. All notices or other communications required or permitted to be given by any party to any other party pursuant to the terms of this Agreement shall be in writing, unless otherwise specified, and if sent to the Agent, shall be delivered to:

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022
Attention: Capital Markets/Jeffrey Lumby
Facsimile: (212) 307-3730

and:

Cantor Fitzgerald & Co.
499 Park Avenue
New York, NY 10022
Attention: General Counsel
Facsimile: (212) 829-4708

with a copy to (such copy not to constitute notice):

Cooley LLP
1114 Avenue of the Americas
New York, NY 10036
Attention: Daniel I. Goldberg, Esq.
Facsimile: (212) 479-6275

and if to the Company, shall be delivered to:

Aerpio Pharmaceuticals, Inc.
9987 Carver Road
Cincinnati, OH 45242
Attention: Stephen Hoffman
Facsimile: (513) 985-0999

with a copy to (such copy not to constitute notice):

Goodwin Procter LLP
100 Northern Avenue
Boston, MA 02210
Attention: Danielle M. Lauzon, Esq. and James Xu, Esq.
Facsimile: (617) 649-1484

Each party to this Agreement may change such address for notices by sending to the parties to this Agreement written notice of a new address for such purpose. Each such notice or other communication shall be deemed given (i) when delivered personally or by verifiable facsimile transmission (with an original to follow) on or before 4:30 p.m., New York City time, on a Business Day or, if such day is not a Business Day, on the next succeeding Business Day, (ii) by Electronic Notice as set forth in the next paragraph, (iii) on the next Business Day after timely delivery to a nationally-recognized overnight courier and (iv) on the Business Day actually received if deposited in the U.S. mail (certified or registered mail, return receipt requested, postage prepaid). For purposes of this Agreement, "**Business Day**" shall mean any day on which the Exchange and commercial banks in the City of New York are open for business.

An electronic communication ("**Electronic Notice**") shall be deemed written notice for purposes of this Section 14 if sent to the electronic mail address specified by the receiving party under separate cover. Electronic Notice shall be deemed received at the time the party sending Electronic Notice receives verification of receipt by the receiving party. Any party receiving Electronic Notice may request and shall be entitled to receive the notice on paper, in a nonelectronic form ("**Nonelectronic Notice**") which shall be sent to the requesting party within ten (10) days of receipt of the written request for Nonelectronic Notice.

15. Successors and Assigns. This Agreement shall inure to the benefit of and be binding upon the Company and the Agent and their respective successors and the parties referred to in Section 11 hereof. References to any of the parties contained in this Agreement shall be deemed to include the successors and permitted assigns of such party. Nothing in this Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective successors and permitted assigns any rights, remedies, obligations or liabilities under or by reason of this Agreement, except as expressly provided in this Agreement. Neither party may assign its rights or obligations under this Agreement without the prior written consent of the other party; *provided*, *however*, that the Agent may assign its rights and obligations hereunder to an affiliate thereof without obtaining the Company's consent so long as such affiliate is a registered broker dealer and the Agent provides notice of such assignment to the Company.

16. Adjustments for Stock Splits. The parties acknowledge and agree that all share-related numbers contained in this Agreement shall be adjusted to take into account any stock split, stock dividend or similar event effected with respect to the Placement Shares.

17. Entire Agreement; Amendment; Severability; Waiver. This Agreement (including all schedules and exhibits attached hereto and Placement Notices issued pursuant hereto) constitutes the entire agreement and supersedes all other prior and contemporaneous agreements and undertakings, both written and oral, among the parties hereto with regard to the subject matter hereof. Neither this Agreement nor any term hereof may be amended except pursuant to a written instrument executed by the Company and the Agent. In the event that any one or more of the provisions contained herein, or the application thereof in any circumstance, is held invalid, illegal or unenforceable as written by a court of competent jurisdiction, then such provision shall be given full force and effect to the fullest possible extent that it is valid, legal and enforceable, and the remainder of the terms and provisions herein shall be construed as if such invalid, illegal or unenforceable term or provision was not contained herein, but only to the extent that giving effect to such provision and the remainder of the terms and provisions hereof shall be in accordance with the intent of the parties as reflected in this Agreement. No implied waiver by a party shall arise in the absence of a waiver in writing signed by such party. No failure or delay in exercising any right, power, or privilege hereunder shall operate as a waiver thereof, nor shall any single or partial exercise thereof preclude any other or further exercise thereof or the exercise of any right, power, or privilege hereunder.

18. **GOVERNING LAW AND TIME; WAIVER OF JURY TRIAL. THIS AGREEMENT SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO THE PRINCIPLES OF CONFLICTS OF LAWS. SPECIFIED TIMES OF DAY REFER TO NEW YORK CITY TIME. EACH PARTY HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED HEREBY.**

19. **CONSENT TO JURISDICTION. EACH PARTY HEREBY IRREVOCABLY SUBMITS TO THE EXCLUSIVE JURISDICTION OF THE STATE AND FEDERAL COURTS SITTING IN THE CITY OF NEW YORK, BOROUGH OF MANHATTAN, FOR THE ADJUDICATION OF ANY DISPUTE HEREUNDER OR IN CONNECTION WITH ANY TRANSACTION CONTEMPLATED HEREBY, AND HEREBY IRREVOCABLY WAIVES, AND AGREES NOT TO ASSERT IN ANY SUIT, ACTION OR PROCEEDING, ANY CLAIM THAT IT IS NOT PERSONALLY SUBJECT TO THE JURISDICTION OF ANY SUCH COURT, THAT SUCH SUIT, ACTION OR PROCEEDING IS BROUGHT IN AN INCONVENIENT FORUM OR THAT THE VENUE OF SUCH SUIT, ACTION OR PROCEEDING IS IMPROPER. EACH PARTY HEREBY IRREVOCABLY WAIVES PERSONAL SERVICE OF PROCESS AND CONSENTS TO PROCESS BEING SERVED IN ANY SUCH SUIT, ACTION OR PROCEEDING BY MAILING A COPY THEREOF (CERTIFIED OR REGISTERED MAIL, RETURN RECEIPT REQUESTED) TO SUCH PARTY AT THE ADDRESS IN EFFECT FOR NOTICES TO IT UNDER THIS AGREEMENT AND AGREES THAT SUCH SERVICE SHALL CONSTITUTE GOOD AND SUFFICIENT SERVICE OF PROCESS AND NOTICE THEREOF. NOTHING CONTAINED HEREIN SHALL BE DEEMED TO LIMIT IN ANY WAY ANY RIGHT TO SERVE PROCESS IN ANY MANNER PERMITTED BY LAW.**

20. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. Delivery of an executed Agreement by one party to the other may be made by facsimile or electronic transmission.

21. Construction. The section and exhibit headings herein are for convenience only and shall not affect the construction hereof. References herein to any law, statute, ordinance, code, regulation, rule or other requirement of any Governmental Authority shall be deemed to refer to such law, statute, ordinance, code, regulation, rule or other requirement of any Governmental Authority as amended, reenacted, supplemented or superseded in whole or in part and in effect from time to time and also to all rules and regulations promulgated thereunder.

22. Permitted Free Writing Prospectuses. The Company represents, warrants and agrees that, unless it obtains the prior written consent of the Agent, and the Agent represents, warrants and agrees that, unless it obtains the prior written consent of the Company, it has not made and will not make any offer relating to the Placement Shares that would constitute an Issuer Free Writing Prospectus, or that would otherwise constitute a "free writing prospectus," as defined in Rule 405, required to be filed with the Commission. Any such free writing prospectus consented to by the Agent or by the Company, as the case may be, is hereinafter referred to as a "Permitted Free Writing Prospectus." The Company represents and warrants that it has treated and agrees that it will treat each Permitted Free Writing Prospectus as an "issuer free writing prospectus," as defined in Rule 433, and has complied and will comply with the requirements of Rule 433 applicable to any Permitted Free Writing Prospectus, including timely filing with the Commission where required, legending and record keeping. For the purposes of clarity, the parties hereto agree that all free writing prospectuses, if any, listed in Exhibit 22 hereto are Permitted Free Writing Prospectuses.

23. Absence of Fiduciary Relationship. The Company acknowledges and agrees that:

(a) the Agent is acting solely as agent in connection with the public offering of the Placement Shares and in connection with each transaction contemplated by this Agreement and the process leading to such transactions, and no fiduciary or advisory relationship between the Company or any of its respective affiliates, stockholders (or other equity holders), creditors or employees or any other party, on the one hand, and the Agent, on the other hand, has been or will be created in respect of any of the transactions contemplated by this Agreement, irrespective of whether or not the Agent has advised or is advising the Company on other matters, and the Agent has no obligation to the Company with respect to the transactions contemplated by this Agreement except the obligations expressly set forth in this Agreement;

(b) it is capable of evaluating and understanding, and understands and accepts, the terms, risks and conditions of the transactions contemplated by this Agreement;

(c) neither the Agent nor its affiliates have provided any legal, accounting, regulatory or tax advice with respect to the transactions contemplated by this Agreement and it has consulted its own legal, accounting, regulatory and tax advisors to the extent it has deemed appropriate;

(d) it is aware that the Agent and its affiliates are engaged in a broad range of transactions which may involve interests that differ from those of the Company and the Agent and its affiliates have no obligation to disclose such interests and transactions to the Company by virtue of any fiduciary, advisory or agency relationship or otherwise; and

(e) it waives, to the fullest extent permitted by law, any claims it may have against the Agent or its affiliates for breach of fiduciary duty or alleged breach of fiduciary duty in connection with the sale of Placement Shares under this Agreement and agrees that the Agent and its affiliates shall not have any liability (whether direct or indirect, in contract, tort or otherwise) to it in respect of such a fiduciary duty claim or to any person asserting a fiduciary duty claim on its behalf or in right of it or the Company, employees or creditors of Company.

24. Definitions. As used in this Agreement, the following terms have the respective meanings set forth below:

"**Applicable Time**" means (i) each Representation Date, (ii) the time of each sale of any Placement Shares pursuant to this Agreement and (iii) each Settlement Date.

"**Governmental Authority**" means (i) any federal, provincial, state, local, municipal, national or international government or governmental authority, regulatory or administrative agency, governmental commission, department, board, bureau, agency or instrumentality, court, tribunal, arbitrator or arbitral body (public or private); (ii) any self-regulatory organization; or (iii) any political subdivision of any of the foregoing.

"**Issuer Free Writing Prospectus**" means any "issuer free writing prospectus," as defined in Rule 433, relating to the Placement Shares that (1) is required to be filed with the Commission by the Company, (2) is a "road show" that is a "written communication" within the meaning of Rule 433(d)(8)(i) whether or not required to be filed with the Commission, or (3) is exempt from filing pursuant to Rule 433(d)(5)(i) because it contains a description of the Placement Shares or of the offering that does not reflect the final terms, in each case in the form filed or required to be filed with the Commission or, if not required to be filed, in the form retained in the Company's records pursuant to Rule 433(g) under the Securities Act Regulations.

"**Rule 164**," "**Rule 172**," "**Rule 405**," "**Rule 415**," "**Rule 424**," "**Rule 424(b)**," "**Rule 430B**," and "**Rule 433**" refer to such rules under the Securities Act Regulations.

All references in this Agreement to financial statements and schedules and other information that is "contained," "included" or "stated" in the Registration Statement or the Prospectus (and all other references of like import) shall be deemed to mean and include all such financial statements and schedules and other information that is incorporated by reference in the Registration Statement or the Prospectus, as the case may be.

All references in this Agreement to the Registration Statement, the Prospectus or any amendment or supplement to any of the foregoing shall be deemed to include the copy filed with the Commission pursuant to EDGAR; all references in this Agreement to any Issuer Free Writing Prospectus (other than any Issuer Free Writing Prospectuses that, pursuant to Rule 433, are not required to be filed with the Commission) shall be deemed to include the copy thereof filed with the Commission pursuant to EDGAR; and all references in this Agreement to "supplements" to the Prospectus shall include, without limitation, any supplements, "wrappers" or similar materials prepared in connection with any offering, sale or private placement of any Placement Shares by the Agent outside of the United States.

[*Signature Page Follows*]

If the foregoing correctly sets forth the understanding between the Company and the Agent, please so indicate in the space provided below for that purpose, whereupon this letter shall constitute a binding agreement between the Company and the Agent.

Very truly yours,

AERPIO PHARMACEUTICALS, INC.

By: /s/ Michael Rogers
Name: Michael Rogers
Title: Chief Financial Officer

ACCEPTED as of the date first-above written:

CANTOR FITZGERALD & CO.

By: /s/ Jeffrey Lumby
Name: Jeffrey Lumby
Title: Senior Managing Director

SCHEDULE 1

Form of Placement Notice

From: Aerpio Pharmaceuticals, Inc.

To: Cantor Fitzgerald & Co. Attention: [●]

Subject: Placement Notice

Date: [●], 201[●]

Ladies and Gentlemen:

Pursuant to the terms and subject to the conditions contained in the Sales Agreement between Aerpio Pharmaceuticals, Inc., a Delaware corporation (the "**Company**"), and Cantor Fitzgerald & Co. ("**Agent**"), dated February 21, 2018, the Company hereby requests that the Agent sell up to [●] of the Company's common stock, par value $0.0001 per share, at a minimum market price of $[●] per share, during the time period beginning [month, day, time] and ending [month, day, time].

SCHEDULE 2

Compensation

The Company shall pay to the Agent in cash, upon each sale of Placement Shares pursuant to this Agreement, an amount up to 3.0% of the aggregate gross proceeds from each sale of Placement Shares.

SCHEDULE 3

Notice Parties

The Company

Mike Rogers (mrogers@Aerpio.com)

Stephen Hoffman (shoffman@Aerpio.com)

Joseph Gardner (jgardner@aerpio.com)

The Agent

Jeffrey Lumby (jlumby@cantor.com)

Joshua Feldman (jfeldman@cantor.com)

Sameer Vasudev (svasudev@cantor.com)

With copies to:

CFControlledEquityOffering@cantor.com

SCHEDULE 4

Subsidiaries

Incorporated by reference to Exhibit 21.1 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, or the Company's most recently filed Annual Report on Form 10-K, as applicable.

Exhibit 22

Permitted Free Writing Prospectus

None.

Exhibit 4.5

AERPIO PHARMACEUTICALS, INC.
Issuer

AND

AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC,
Trustee

INDENTURE

Dated as of [●]

Subordinated Debt Securities

TABLE OF CONTENTS

(1) This Table of Contents does not constitute part of the Indenture and shall not have any bearing on the interpretation of any of its terms or provisions.

INDENTURE

INDENTURE, dated as of [•], among **AERPIO PHARMACEUTICALS, INC.**, a Delaware corporation (the "Company"), and **AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC,** as trustee (the "Trustee"):

WHEREAS, for its lawful corporate purposes, the Company has duly authorized the execution and delivery of this Indenture to provide for the issuance of subordinated debt securities (hereinafter referred to as the "Securities"), in an unlimited aggregate principal amount to be issued from time to time in one or more series as in this Indenture provided, as registered Securities without coupons, to be authenticated by the certificate of the Trustee;

WHEREAS, to provide the terms and conditions upon which the Securities are to be authenticated, issued and delivered, the Company has duly authorized the execution of this Indenture; and

WHEREAS, all things necessary to make this Indenture a valid agreement of the Company, in accordance with its terms, have been done.

NOW, THEREFORE, in consideration of the premises and the purchase of the Securities by the holders thereof, it is mutually covenanted and agreed as follows for the equal and ratable benefit of the holders of Securities:

ARTICLE 1

DEFINITIONS

Section 1.01 Definitions of Terms. The terms defined in this Section (except as in this Indenture or any indenture supplemental hereto otherwise expressly provided or unless the context otherwise requires) for all purposes of this Indenture and of any indenture supplemental hereto shall have the respective meanings specified in this Section and shall include the plural as well as the singular. All other terms used in this Indenture that are defined in the Trust Indenture Act of 1939, as amended, or that are by reference in such Act defined in the Securities Act of 1933, as amended (except as herein or any indenture supplemental hereto otherwise expressly provided or unless the context otherwise requires), shall have the meanings assigned to such terms in said Trust Indenture Act and in said Securities Act as in force at the date of the execution of this instrument.

"***Authenticating Agent***" means an authenticating agent with respect to all or any of the series of Securities appointed by the Trustee pursuant to Section 2.10.

"***Bankruptcy Law***" means Title 11, U.S. Code, or any similar federal or state law for the relief of debtors.

"***Board of Directors***" means the Board of Directors (or the functional equivalent thereof) of the Company or any duly authorized committee of such Board.

"***Board Resolution***" means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company to have been duly adopted by the Board of Directors and to be in full force and effect on the date of such certification.

"***Business Day***" means, with respect to any series of Securities, any day other than a day on which federal or state banking institutions in the Borough of Manhattan, the City of New York, or in the city of the Corporate Trust Office of the Trustee, are authorized or obligated by law, executive order or regulation to close.

"***Certificate***" means a certificate signed by any Officer. The Certificate need not comply with the provisions of Section 13.07.

"***Commission***" means the Securities and Exchange Commission, as from time to time constituted, created under the Exchange Act, or, if at any time after the execution of this instrument such Commission is not existing and performing the duties now assigned to it under the Trust Indenture Act, then the body performing such duties at such time.

"***Company***" means Aerpio Pharmaceuticals, Inc., a corporation duly organized and existing under the laws of the State of Delaware, and, subject to the provisions of Article Ten, shall also include its successors and assigns.

"***Corporate Trust Office***" means the office of the Trustee at which, at any particular time, its corporate trust business shall be principally administered, which office at the date hereof is located at 6201 15th Avenue, Brooklyn, New York 11219.

"***Custodian***" means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

"***Defaulted Interest***" has the meaning set forth in Section 2.03.

"***Depositary***" means, with respect to Securities of any series for which the Company shall determine that such Securities will be issued as a Global Security, The Depository Trust Company, another clearing agency, or any successor registered as a clearing agency under the Exchange Act, or other applicable statute or regulation, which, in each case, shall be designated by the Company pursuant to either Section 2.01 or 2.11.

"***Event of Default***" means, with respect to Securities of a particular series, any event specified in Section 6.01, continued for the period of time, if any, therein designated.

"***Exchange Act***" means the United States Securities and Exchange Act of 1934, as amended, and the rules and regulations promulgated by the Commission thereunder.

"***Global Security***" means a Security issued to evidence all or a part of any series of Securities which is executed by the Company and authenticated and delivered by the Trustee to the Depositary or pursuant to the Depositary's instruction, all in accordance with the Indenture, which shall be registered in the name of the Depositary or its nominee.

"***Governmental Obligations***" means securities that are (a) direct obligations of the United States of America for the payment of which its full faith and credit is pledged or (b) obligations of a Person controlled or supervised by and acting as an agency or instrumentality of the United States of America, the payment of which is unconditionally guaranteed as a full faith and credit obligation by the United States of America that, in either case, are not callable or redeemable at the option of the issuer thereof at any time prior to the stated maturity of the Securities, and shall also include a depositary receipt issued by a bank or trust company as custodian with respect to any such Governmental Obligation or a specific payment of principal of or interest on any such Governmental Obligation held by such custodian for the account of the holder of such depositary receipt; *provided*, *however*, that (except as required by law) such custodian is not authorized to make any deduction from the amount payable to the holder of such depositary receipt from any amount received by the custodian in respect of the Governmental Obligation or the specific payment of principal of or interest on the Governmental Obligation evidenced by such depositary receipt.

"***herein***", "***hereof***" and "***hereunder***", and other words of similar import, refer to this Indenture as a whole and not to any particular Article, Section or other subdivision.

"***Indenture***" means this instrument as originally executed or as it may from time to time be supplemented or amended by one or more indentures supplemental hereto entered into in accordance with the terms hereof and shall include the terms of particular series of Securities established as contemplated by Section 2.01.

"***Interest Payment Date***", when used with respect to any installment of interest on a Security of a particular series, means the date specified in such Security or in a Board Resolution or in an indenture supplemental hereto with respect to such series as the fixed date on which an installment of interest with respect to Securities of that series is due and payable.

"***Officer***" means, with respect to the Company, the chairman of the Board of Directors, a chief executive officer, a president, a chief financial officer, a chief operating officer, any executive vice president, any senior vice president, any vice president, the treasurer or any assistant treasurer, the controller or any assistant controller or the secretary or any assistant secretary.

"***Officer's Certificate***" means a certificate signed by any Officer. Each such certificate shall include the statements provided for in Section 13.07, if and to the extent required by the provisions thereof.

"***Opinion of Counsel***" means an opinion in writing subject to customary exceptions of legal counsel, who may be an employee of or counsel for the Company, that is delivered to the Trustee in accordance with the terms hereof. Each such opinion shall include the statements provided for in Section 13.07, if and to the extent required by the provisions thereof.

"***Outstanding***", when used with reference to Securities of any series, means, subject to the provisions of Section 8.04, as of any particular time, all Securities of that series theretofore authenticated and delivered by the Trustee under this Indenture, except (a) Securities theretofore canceled by the Trustee or any paying agent, or delivered to the Trustee or any paying agent for cancellation or that have previously been canceled; (b) Securities or portions thereof for the payment or redemption of which moneys or Governmental Obligations in the necessary amount shall have been deposited in trust with the Trustee or with any paying agent (other than the Company) or shall have been set aside and segregated in trust by the Company (if the Company shall act as its own paying agent); *provided*, *however*, that if such Securities or portions of such Securities are to be redeemed prior to the maturity thereof, notice of such redemption shall have been given as provided in Article Three, or provision satisfactory to the Trustee shall have been made for giving such notice; and (c) Securities in lieu of or in substitution for which other Securities shall have been authenticated and delivered pursuant to the terms of Section 2.07.

"***Person***" means any individual, corporation, partnership, joint venture, joint-stock company, limited liability company, association, trust, unincorporated organization, any other entity or organization, including a government or political subdivision or an agency or instrumentality thereof.

"***Predecessor Security***" of any particular Security means every previous Security evidencing all or a portion of the same debt as that evidenced by such particular Security; and, for the purposes of this definition, any Security authenticated and delivered under Section 2.07 in lieu of a lost, destroyed or stolen Security shall be deemed to evidence the same debt as the lost, destroyed or stolen Security.

"***Responsible Officer***" when used with respect to the Trustee means any officer of the Trustee assigned by the Trustee to administer its corporate trust matters with respect to this Indenture (which, for the avoidance of doubt, includes without limitation any supplemental indenture hereto).

"***Securities***" has the meaning stated in the first recital of this Indenture and more particularly means any Securities authenticated and delivered under this Indenture.

"***Securityholder***", "***holder of Securities***", "***registered holder***", or other similar term, means the Person or Persons in whose name or names a particular Security is registered on the Security Register kept for that purpose in accordance with the terms of this Indenture.

"***Security Register***" and "***Security Registrar***" shall have the meanings as set forth in Section 2.05.

"***Subsidiary***" means, with respect to any Person:

(1) any corporation or company a majority of whose capital stock with voting power, under ordinary circumstances, to elect directors is, at the date of determination, directly or indirectly, owned by such Person (a "***subsidiary***"), by one or more subsidiaries of such Person or by such Person and one or more subsidiaries of such Person;

(2) a partnership in which such Person or a subsidiary of such Person is, at the date of determination, a general partner of such partnership; or

(3) any partnership, limited liability company or other Person in which such Person, a subsidiary of such Person or such Person and one or more subsidiaries of such Person, directly or indirectly, at the date of determination, have (x) at least a majority ownership interest or (y) the power to elect or appoint or direct the election or appointment of the managing partner or member of such Person or, if applicable, a majority of the directors or other governing body of such Person.

"***Trustee***" means American Stock Transfer & Trust Company, LLC, and, subject to the provisions of Article Seven, shall also include its successors and assigns, and, if at any time there is more than one Person acting in such capacity hereunder, "Trustee" shall mean each such Person. The term "Trustee" as used with respect to a particular series of the Securities shall mean the trustee with respect to that series.

"***Trust Indenture Act***" means the Trust Indenture Act of 1939, as amended.

ARTICLE 2

ISSUE, DESCRIPTION, TERMS, EXECUTION, REGISTRATION AND EXCHANGE OF SECURITIES

Section 2.01 Designation and Terms of Securities.

(1) The aggregate principal amount of Securities that may be authenticated and delivered under this Indenture is unlimited. The Securities may be issued in one or more series up to the aggregate principal amount of Securities of that series from time to time authorized by or pursuant to a Board Resolution or pursuant to one or more indentures supplemental hereto. Prior to the initial issuance of Securities of any series, there shall be established in or pursuant to a Board Resolution, and set forth in an Officer's Certificate, or established in one or more indentures supplemental hereto:

(a) the title of the Securities of the series (which shall distinguish the Securities of that series from all other Securities);

(b) any limit upon the aggregate principal amount of the Securities of that series which may be authenticated and delivered under this Indenture (except for Securities authenticated and delivered upon registration of transfer of, or in exchange for, or in lieu of, other Securities of that series);

(c) the date or dates on which the principal of the Securities of the series is payable;

(d) if the price (expressed as a percentage of the aggregate principal amount thereof) at which such Securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such Securities that is convertible into another security or the method by which any such portion shall be determined;

(e) the rate or rates at which the Securities of the series shall bear interest or the manner of calculation of such rate or rates, if any;

(f) the date or dates from which such interest shall accrue, the Interest Payment Dates on which such interest will be payable or the manner of determination of such Interest Payment Dates, the place(s) of payment, and the record date for the determination of holders to whom interest is payable on any such Interest Payment Dates or the manner of determination of such record dates;

(g) the right, if any, to extend the interest payment periods and the duration of such extension;

(h) the period or periods within which, the price or prices at which and the terms and conditions upon which Securities of the series may be redeemed, converted or exchanged, in whole or in part;

(i) the obligation, if any, of the Company to redeem or purchase Securities of the series pursuant to any sinking fund, mandatory redemption, or analogous provisions (including payments made in cash in satisfaction of future sinking fund obligations) or at the option of a holder thereof and the period or periods within which, the price or prices at which, and the terms and conditions upon which, Securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

(j) the form of the Securities of the series including the form of the Certificate of Authentication for such series;

(k) if other than denominations of one thousand U.S. dollars ($1,000) or any integral multiple thereof, the denominations in which the Securities of the series shall be issuable;

(l) any and all other terms (including terms, to the extent applicable, relating to any auction or remarketing of the Securities of that series and any security for the obligations of the Company with respect to such Securities) with respect to such series (which terms shall not be inconsistent with the terms of this Indenture, as amended by any supplemental indenture) including any terms which may be required by or advisable under United States laws or regulations or advisable in connection with the marketing of Securities of that series;

(m) whether the Securities of the series shall be issued in whole or in part in the form of a Global Security or Securities; the terms and conditions, if any, upon which such Global Security or Securities may be exchanged in whole or in part for other individual Securities; and the Depositary for such Global Security or Securities;

(n) whether the Securities will be convertible into or exchangeable for shares of common stock, preferred stock or other securities of the Company or any other Person and, if so, the terms and conditions upon which such Securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at the Company's option or the holders' option) conversion or exchange features, and the applicable conversion or exchange period;

(o) if other than the full principal amount thereof, the portion of the principal amount of Securities of the series which shall be payable upon declaration of acceleration of the maturity thereof pursuant to Section 6.01;

(p) any additional or alternative events of default;

(q) additional or alternative covenants (which may include, among other restrictions, restrictions on the Company's ability or the ability of the Company's Subsidiaries to: incur additional indebtedness; issue additional securities; create liens; pay dividends or make distributions in respect of the capital stock of the Company or the Company's Subsidiaries; redeem capital stock; place restrictions on the Company's Subsidiaries' ability to pay dividends, make distributions or transfer assets; make investments or other restricted payments; sell or otherwise dispose of assets; enter into sale-leaseback transactions; engage in transactions with stockholders or affiliates; issue or sell stock of the Company's Subsidiaries; or effect a consolidation or merger) or financial covenants (which may include, among other financial covenants, financial covenants that require the Company and its Subsidiaries to maintain specified interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios) provided for with respect to the Securities of the series;

(r) the currency or currencies, including composite currencies, in which payment of the principal of (and premium, if any) and interest, if any, on such Securities shall be payable (if other than the currency of the United States of America), which unless otherwise specified shall be the currency of the United States of America as at the time of payment is legal tender for payment of public or private debts;

(s) if the principal of (and premium, if any) or interest, if any, on such Securities is to be payable, at the election of the Company or any Holder thereof, in a coin or currency other than that in which such Securities are stated to be payable, then the period or periods within which, and the terms and conditions upon which, such election may be made;

(t) whether interest will be payable in cash or additional Securities at the Company's or the Securityholders' option and the terms and conditions upon which the election may be made;

(u) the terms and conditions, if any, upon which the Company shall pay amounts in addition to the stated interest, premium, if any and principal amounts of the Securities of the series to any Securityholder that is not a "United States person" for federal tax purposes;

(v) additional or alternative provisions, if any, related to defeasance and discharge of the offered Securities;

(w) the applicability of any guarantees;

(x) any restrictions on transfer, sale or assignment of the Securities of the series;

(y) any other terms of the series; and

(z) the subordination terms of the Securities of the series.

All Securities of any one series shall be substantially identical except as may otherwise be provided in or pursuant to any such Board Resolution or in any indentures supplemental hereto.

If any of the terms of the series are established by action taken pursuant to a Board Resolution of the Company, a copy of an appropriate record of such action shall be certified by the secretary or an assistant secretary of the Company and delivered to the Trustee at or prior to the delivery of the Officer's Certificate of the Company setting forth the terms of the series.

Securities of any particular series may be issued at various times, with different dates on which the principal or any installment of principal is payable, with different rates of interest, if any, or different methods by which rates of interest may be determined, with different dates on which such interest may be payable and with different redemption dates.

Section 2.02 Form of Securities and Trustee's Certificate. The Securities of any series and the Trustee's certificate of authentication to be borne by such Securities shall be substantially of the tenor and purport as set forth in one or more indentures supplemental hereto or as provided in a Board Resolution, and set forth in an Officer's Certificate, and they may have such letters, numbers or other marks of identification or designation and such legends or endorsements printed, lithographed or engraved thereon as the Company may deem appropriate and as are not inconsistent with the provisions of this Indenture, or as may be required to comply with any law or with any rule or regulation made pursuant thereto or with any rule or regulation of any securities exchange on which Securities of that series may be listed, or to conform to usage.

Section 2.03 Denominations: Provisions for Payment. The Securities shall be issuable as registered Securities and in the denominations of one thousand U.S. dollars ($1,000) or any integral multiple thereof, subject to Section 2.01(1)(j). The Securities of a particular series shall bear interest payable on the dates and at the rate specified with respect to that series. Subject to Section 2.01(1)(p), the principal of and the interest on the Securities of any series, as well as any premium thereon in case of redemption thereof prior to maturity, shall be payable in the coin or currency of the United States of America that at the time is legal tender for public and private debt, at the office or agency of the Company maintained for that purpose. Each Security shall be dated the date of its authentication. Interest on the Securities shall be computed on the basis of a 360-day year composed of twelve 30-day months.

The interest installment on any Security that is payable, and is punctually paid or duly provided for, on any Interest Payment Date for Securities of that series shall be paid to the Person in whose name said Security (or one or more Predecessor Securities) is registered at the close of business on the regular record date for such interest installment. In the event that any Security of a particular series or portion thereof is called for redemption and the redemption date is subsequent to a regular record date with respect to any Interest Payment Date and prior to such Interest Payment Date, interest on such Security will be paid upon presentation and surrender of such Security as provided in Section 3.03.

Any interest on any Security that is payable, but is not punctually paid or duly provided for, on any Interest Payment Date for Securities of the same series (herein called "Defaulted Interest") shall forthwith cease to be payable to the registered holder on the relevant regular record date by virtue of having been such holder; and such Defaulted Interest shall be paid by the Company, at its election, as provided in clause (1) or clause (2) below:

(1) The Company may make payment of any Defaulted Interest on Securities to the Persons in whose names such Securities (or their respective Predecessor Securities) are registered at the close of business on a special record date for the payment of such Defaulted Interest, which shall be fixed in the following manner: the Company shall notify the Trustee in writing of the amount of Defaulted Interest proposed to be paid on each such Security and the date of the proposed payment, and at the same time the Company shall deposit with the Trustee an amount of money equal to the aggregate amount proposed to be paid in respect of such Defaulted Interest or shall make arrangements satisfactory to the Trustee for such deposit prior to the date of the proposed payment, such money when deposited to be held in trust for the benefit of the Persons entitled to such Defaulted Interest as in this clause provided. Thereupon the Trustee shall fix a special record date for the payment of such Defaulted Interest which shall not be more than 15 nor less than 10 days prior to the date of the proposed payment and not less than 10 days after the receipt by the Trustee of the notice of the proposed payment. The Trustee shall promptly notify the Company of such special record date and, in the name and at the expense of the Company, shall cause notice of the proposed payment of such Defaulted Interest and the special record date therefor to be mailed, first class postage prepaid, to each Securityholder at his or her address as it appears in the Security Register (as hereinafter defined), not less than 10 days prior to such special record date. Notice of the proposed payment of such Defaulted Interest and the special record date therefor having been mailed as aforesaid, such Defaulted Interest shall be paid to the Persons in whose names such Securities (or their respective Predecessor Securities) are registered on such special record date.

(2) The Company may make payment of any Defaulted Interest on any Securities in any other lawful manner not inconsistent with the requirements of any securities exchange on which such Securities may be listed, and upon such notice as may be required by such exchange, if, after notice given by the Company to the Trustee of the proposed payment pursuant to this clause, such manner of payment shall be deemed practicable by the Trustee.

Unless otherwise set forth in a Board Resolution or one or more indentures supplemental hereto establishing the terms of any series of Securities pursuant to Section 2.01 hereof, the term "regular record date" as used in this Section with respect to a series of Securities and any Interest Payment Date for such series shall mean either the fifteenth day of the month immediately preceding the month in which an Interest Payment Date established for such series pursuant to Section 2.01 hereof shall occur, if such Interest Payment Date is the first day of a month, or the first day of the month in which an Interest Payment Date established for such series pursuant to Section 2.01 hereof shall occur, if such Interest Payment Date is the fifteenth day of a month, whether or not such date is a Business Day.

Subject to the foregoing provisions of this Section, each Security of a series delivered under this Indenture upon transfer of or in exchange for or in lieu of any other Security of such series shall carry the rights to interest accrued and unpaid, and to accrue, that were carried by such other Security.

Section 2.04 Execution and Authentications. The Securities shall be signed on behalf of the Company by one of its Officers. Signatures may be in the form of a manual or facsimile signature.

The Company may use the facsimile signature of any Person who shall have been an Officer, notwithstanding the fact that at the time the Securities shall be authenticated and delivered or disposed of such Person shall have ceased to be such an officer of the Company. The Securities may contain such notations, legends or endorsements required by law, stock exchange rule or usage. Each Security shall be dated the date of its authentication by the Trustee.

A Security shall not be valid until authenticated manually by an authorized signatory of the Trustee, or by an Authenticating Agent. Such signature shall be conclusive evidence that the Security so authenticated has been duly authenticated and delivered hereunder and that the holder is entitled to the benefits of this Indenture. At any time and from time to time after the execution and delivery of this Indenture, the Company may deliver Securities of any series executed by the Company to the Trustee for authentication, together with a written order of the Company for the authentication and delivery of such Securities, signed by an Officer, and the Trustee in accordance with such written order shall authenticate and deliver such Securities.

In authenticating such Securities and accepting the additional responsibilities under this Indenture in relation to such Securities, the Trustee shall be entitled to receive, if requested, and (subject to Section 7.01) shall be fully protected in relying upon, an Opinion of Counsel stating that the form and terms thereof have been established in conformity with the provisions of this Indenture.

The Trustee shall not be required to authenticate such Securities if the issue of such Securities pursuant to this Indenture will affect the Trustee's own rights, duties or immunities under the Securities and this Indenture or otherwise in a manner that is not reasonably acceptable to the Trustee.

Section 2.05 Registration of Transfer and Exchange.

(1) Securities of any series may be exchanged upon presentation thereof at the office or agency of the Company designated for such purpose, for other Securities of such series of authorized denominations, and for a like aggregate principal amount, upon payment of a sum sufficient to cover any tax or other governmental charge in relation thereto, all as provided in this Section. In respect of any Securities so surrendered for exchange, the Company shall execute, the Trustee shall authenticate and such office or agency shall deliver in exchange therefor the Security or Securities of the same series that the Securityholder making the exchange shall be entitled to receive, bearing numbers not contemporaneously outstanding.

(2) The Company shall keep, or cause to be kept, at its office or agency designated for such purpose a register or registers (herein referred to as the "Security Register") in which, subject to such reasonable regulations as it may prescribe, the Company shall register the Securities and the transfers of Securities as in this Article provided and which at all reasonable times shall be open for inspection by the Trustee. The registrar for the purpose of registering Securities and transfer of Securities as herein provided shall be appointed as authorized by Board Resolution (the "Security Registrar").

Upon surrender for transfer of any Security at the office or agency of the Company designated for such purpose, the Company shall execute, the Trustee shall authenticate and such office or agency shall deliver in the name of the transferee or transferees a new Security or Securities of the same series as the Security presented for a like aggregate principal amount.

All Securities presented or surrendered for exchange or registration of transfer, as provided in this Section, shall be accompanied (if so required by the Company or the Security Registrar) by a written instrument or instruments of transfer, in form satisfactory to the Company or the Security Registrar, duly executed by the registered holder or by such holder's duly authorized attorney in writing.

(3) Except as provided pursuant to Section 2.01 pursuant to a Board Resolution, and set forth in an Officer's Certificate, or established in one or more indentures supplemental to this Indenture, no service charge shall be made for any exchange or registration of transfer of Securities, or issue of new Securities in case of partial redemption of any series, but the Company may require payment of a sum sufficient to cover any tax or other governmental charge in relation thereto, other than exchanges pursuant to Section 2.06, Section 3.03(2) and Section 9.04 not involving any transfer.

(4) The Company shall not be required (i) to issue, exchange or register the transfer of any Securities during a period beginning at the opening of business 15 days before the day of the mailing of a notice of redemption of less than all the Outstanding Securities of the same series and ending at the close of business on the day of such mailing, nor (ii) to register the transfer of or exchange any Securities of any series or portions thereof called for redemption, other than the unredeemed portion of any such Securities being redeemed in part. The provisions of this Section 2.05 are, with respect to any Global Security, subject to Section 2.11 hereof.

The Trustee shall have no obligation or duty to monitor, determine or inquire as to compliance with any restrictions on transfer imposed under this Indenture or under applicable law with respect to any transfer of any interest in any Security (including any transfers between or among depositary participants or beneficial owners of interests in any Global Security) other than to require delivery of such certificates and other documentation or evidence as are expressly required by, and to do so if and when expressly required by the terms of, this Indenture, and to examine the same to determine substantial compliance as to form with the express requirements hereof.

Section 2.06 Temporary Securities. Pending the preparation of definitive Securities of any series, the Company may execute, and the Trustee shall authenticate and deliver, temporary Securities (printed, lithographed or typewritten) of any authorized denomination. Such temporary Securities shall be substantially in the form of the definitive Securities in lieu of which they are issued, but with such omissions, insertions and variations as may be appropriate for temporary Securities, all as may be determined by the Company. Every temporary Security of any series shall be executed by the Company and be authenticated by the Trustee upon the same conditions and in substantially the same manner, and with like effect, as the definitive Securities of such series. Without unnecessary delay the Company will execute and will furnish definitive Securities of such series and thereupon any or all temporary Securities of such series may be surrendered in exchange therefor (without charge to the holders), at the office or agency of the Company designated for the purpose, and the Trustee shall authenticate and such office or agency shall deliver in exchange for such temporary Securities an equal aggregate principal amount of definitive Securities of such series, unless the Company advises the Trustee to the effect that definitive Securities need not be executed and furnished until further notice from the Company. Until so exchanged, the temporary Securities of such series shall be entitled to the same benefits under this Indenture as definitive Securities of such series authenticated and delivered hereunder.

Section 2.07 Mutilated, Destroyed, Lost or Stolen Securities. In case any temporary or definitive Security shall become mutilated or be destroyed, lost or stolen, the Company (subject to the next succeeding sentence) shall execute, and upon the Company's request the Trustee (subject as aforesaid) shall authenticate and deliver, a new Security of the same series, bearing a number not contemporaneously outstanding, in exchange and substitution for the mutilated Security, or in lieu of and in substitution for the Security so destroyed, lost or stolen. In every case the applicant for a substituted Security shall furnish to the Company and the Trustee such security or indemnity as may be required by them to save each of them harmless, and, in every case of destruction, loss or theft, the applicant shall also furnish to the Company and the Trustee evidence to their satisfaction of the destruction, loss or theft of the applicant's Security and of the ownership thereof. The Trustee may authenticate any such substituted Security and deliver the same upon the written request or authorization of any officer of the Company. Upon the issuance of any substituted Security, the Company may require the payment of a sum sufficient to cover any tax or other governmental charge that may be imposed in relation thereto and any other expenses (including the fees and expenses of the Trustee) connected therewith.

In case any Security that has matured or is about to mature shall become mutilated or be destroyed, lost or stolen, the Company may, instead of issuing a substitute Security, pay or authorize the payment of the same (without surrender thereof except in the case of a mutilated Security) if the applicant for such payment shall furnish to the Company and the Trustee such security or indemnity as they may require to save them harmless, and, in case of destruction, loss or theft, evidence to the satisfaction of the Company and the Trustee of the destruction, loss or theft of such Security and of the ownership thereof.

Every replacement Security issued pursuant to the provisions of this Section shall constitute an additional contractual obligation of the Company whether or not the mutilated, destroyed, lost or stolen Security shall be found at any time, or be enforceable by anyone, and shall be entitled to all the benefits of this Indenture equally and proportionately with any and all other Securities of the same series duly issued hereunder. All Securities shall be held and owned upon the express condition that the foregoing provisions are exclusive with respect to the

replacement or payment of mutilated, destroyed, lost or stolen Securities, and shall preclude (to the extent lawful) any and all other rights or remedies, notwithstanding any law or statute existing or hereafter enacted to the contrary with respect to the replacement or payment of negotiable instruments or other securities without their surrender.

Section 2.08 Cancellation. All Securities surrendered for the purpose of payment, redemption, exchange or registration of transfer shall, if surrendered to the Company or any paying agent, be delivered to the Trustee for cancellation, or, if surrendered to the Trustee, shall be cancelled by it, and no Securities shall be issued in lieu thereof except as expressly required or permitted by any of the provisions of this Indenture. On request of the Company at the time of such surrender, the Trustee shall deliver to the Company canceled Securities held by the Trustee. In the absence of such request the Trustee may dispose of canceled Securities in accordance with its standard procedures and deliver a certificate of disposition to the Company. If the Company shall otherwise acquire any of the Securities, however, such acquisition shall not operate as a redemption or satisfaction of the indebtedness represented by such Securities unless and until the same are delivered to the Trustee for cancellation.

Section 2.09 Benefits of Indenture. Nothing in this Indenture or in the Securities, express or implied, shall give or be construed to give to any Person, other than the parties hereto and the holders of the Securities (and, with respect to the provisions of Article Fourteen, the holders of any indebtedness of the Company to which the Securities of any series are subordinated) any legal or equitable right, remedy or claim under or in respect of this Indenture, or under any covenant, condition or provision herein contained; all such covenants, conditions and provisions being for the sole benefit of the parties hereto and of the holders of the Securities (and, with respect to the provisions of Article Fourteen, the holders of any indebtedness of the Company to which the Securities of any series are subordinated).

Section 2.10 Authenticating Agent. So long as any of the Securities of any series remain Outstanding there may be an Authenticating Agent for any or all such series of Securities which the Trustee shall have the right to appoint. Said Authenticating Agent shall be authorized to act on behalf of the Trustee to authenticate Securities of such series issued upon exchange, transfer or partial redemption thereof, and Securities so authenticated shall be entitled to the benefits of this Indenture and shall be valid and obligatory for all purposes as if authenticated by the Trustee hereunder. All references in this Indenture to the authentication of Securities by the Trustee shall be deemed to include authentication by an Authenticating Agent for such series. Each Authenticating Agent shall be acceptable to the Company and shall be a corporation that has a combined capital and surplus, as most recently reported or determined by it, sufficient under the laws of any jurisdiction under which it is organized or in which it is doing business to conduct a trust business, and that is otherwise authorized under such laws to conduct such business and is subject to supervision or examination by federal or state authorities. If at any time any Authenticating Agent shall cease to be eligible in accordance with these provisions, it shall resign immediately.

Any Authenticating Agent may at any time resign by giving written notice of resignation to the Trustee and to the Company. The Trustee may at any time (and upon request by the Company shall) terminate the agency of any Authenticating Agent by giving written notice of termination to such Authenticating Agent and to the Company. Upon resignation, termination or cessation of eligibility of any Authenticating Agent, the Trustee may appoint an eligible successor Authenticating Agent acceptable to the Company. Any successor Authenticating Agent, upon acceptance of its appointment hereunder, shall become vested with all the rights, powers and duties of its predecessor hereunder as if originally named as an Authenticating Agent pursuant hereto.

Section 2.11 Global Securities.

(1) If the Company shall establish pursuant to Section 2.01 that the Securities of a particular series are to be issued as a Global Security, then the Company shall execute and the Trustee shall, in accordance with Section 2.04, authenticate and deliver, a Global Security that (i) shall represent, and shall be denominated in an amount equal to the aggregate principal amount of, all of the Outstanding Securities of such series, (ii) shall be registered in the name of the Depositary or its nominee, (iii) shall be delivered by the Trustee to the Depositary or pursuant to the Depositary's instruction and (iv) shall bear a legend substantially to the following effect: "Except as otherwise provided in Section 2.11 of the Indenture, this Security may be transferred, in whole but not in part, only to another nominee of the Depositary or to a successor Depositary or to a nominee of such successor Depositary."

(2) Notwithstanding the provisions of Section 2.05, the Global Security of a series may be transferred, in whole but not in part and in the manner provided in Section 2.05, only to another nominee of the Depositary for such series, or to a successor Depositary for such series selected or approved by the Company or to a nominee of such successor Depositary.

(3) If at any time the Depositary for a series of the Securities notifies the Company that it is unwilling or unable to continue as Depositary for such series or if at any time the Depositary for such series shall no longer be registered or in good standing under the Exchange Act, or other applicable statute or regulation, and a successor Depositary for such series is not appointed by the Company within 90 days after the Company receives such notice or becomes aware of such condition, as the case may be, or if an Event of Default has occurred and is continuing and the Company has received a request from the Depositary or from the Trustee, this Section 2.11 shall no longer be applicable to the Securities of such series and the Company will execute, and subject to Section 2.04, the Trustee will authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security. In addition, the Company may at any time determine that the Securities of any series shall no longer be represented by a Global Security and that the provisions of this Section 2.11 shall no longer apply to the Securities of such series. In such event the Company will execute and, subject to Section 2.04, the Trustee, upon receipt of an Officer's Certificate evidencing such determination by the Company, will authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security. Upon the exchange of the Global Security for such Securities in definitive registered form without coupons, in authorized denominations, the Global Security shall be canceled by the Trustee. Such Securities in definitive registered form issued in exchange for the Global Security pursuant to this Section 2.11(3) shall be registered in such names and in such authorized denominations as the Depositary, pursuant to instructions from its direct or indirect participants or otherwise, shall instruct the Trustee. The Trustee shall deliver such Securities to the Depositary for delivery to the Persons in whose names such Securities are so registered.

ARTICLE 3

REDEMPTION OF SECURITIES AND SINKING FUND PROVISIONS

Section 3.01 Redemption. The Company may redeem the Securities of any series issued hereunder on and after the dates and in accordance with the terms established for such series pursuant to Section 2.01 hereof.

Section 3.02 Notice of Redemption.

(1) In case the Company shall desire to exercise such right to redeem all or, as the case may be, a portion of the Securities of any series in accordance with any right the Company reserved for itself to do so pursuant to Section 2.01 hereof, the Company shall, or shall cause the Trustee to, give notice of such redemption to holders of the Securities of such series to be redeemed by mailing, first class postage prepaid, a notice of such redemption not less than 30 days and not more than 90 days before the date fixed for redemption of that series to such holders at their last addresses as they shall appear upon the Security Register, unless a shorter period is specified in the Securities to be redeemed. Any notice that is mailed in the manner herein provided shall be conclusively presumed to have been duly given, whether or not the registered holder receives the notice. In any case, failure duly to give such notice to the holder of any Security of any series designated for redemption in whole or in part, or any defect in the notice, shall not affect the validity of the proceedings for the redemption of any other Securities of such series or any other series. In the case of any redemption of Securities prior to the expiration of any restriction on such redemption provided in the terms of such Securities or elsewhere in this Indenture, the Company shall furnish the Trustee with an Officer's Certificate evidencing compliance with any such restriction.

Each such notice of redemption shall specify the date fixed for redemption and the redemption price at which Securities of that series are to be redeemed, and shall state that payment of the redemption price of such Securities to be redeemed will be made at the office or agency of the Company, upon presentation and surrender of such Securities, that interest accrued to the date fixed for redemption will be paid as specified in said notice, that from and after said date interest will cease to accrue and that the redemption is from a sinking fund, if such is the case. If less than all the Securities of a series are to be redeemed, the notice to the holders of Securities of that series to be redeemed in part shall specify the particular Securities to be so redeemed.

In case any Security is to be redeemed in part only, the notice that relates to such Security shall state the portion of the principal amount thereof to be redeemed, and shall state that on and after the redemption date, upon surrender of such Security, a new Security or Securities of such series in principal amount equal to the unredeemed portion thereof will be issued.

(2) If less than all the Securities of a series are to be redeemed, the Company shall give the Trustee at least 45 days' notice (unless a shorter notice shall be satisfactory to the Trustee) in advance of the date fixed for redemption as to the aggregate principal amount of Securities of the series to be redeemed, and thereupon the Trustee shall select, by lot or in such other manner as it shall deem appropriate and fair in its discretion and that may provide for the selection of a portion or portions (equal to one thousand U.S. dollars ($1,000) or any integral multiple thereof) of the principal amount of such Securities of a denomination larger than $1,000, the Securities to be redeemed and shall thereafter promptly notify the Company in writing of the numbers of the Securities to be redeemed, in whole or in part. The Company may, if and whenever it shall so elect, by delivery of instructions signed on its behalf by an Officer, instruct the Trustee or any paying agent to call all or any part of the Securities of a particular series for redemption and to give notice of redemption in the manner set forth in this Section, such notice to be in the name of the Company or its own name as the Trustee or such paying agent may deem advisable. In any case in which notice of redemption is to be given by the Trustee or any such paying agent, the Company shall deliver or cause to be delivered to, or permit to remain with, the Trustee or such paying agent, as the case may be, such Security Register, transfer books or other records, or suitable copies or extracts therefrom, sufficient to enable the Trustee or such paying agent to give any notice by mail that may be required under the provisions of this Section.

Section 3.03 Payment Upon Redemption.

(1) If the giving of notice of redemption shall have been completed as above provided, the Securities or portions of Securities of the series to be redeemed specified in such notice shall become due and payable on the date and at the place stated in such notice at the applicable redemption price, together with interest accrued to the date fixed for redemption and interest on such Securities or portions of Securities shall cease to accrue on and after the date fixed for redemption, unless the Company shall default in the payment of such redemption price and accrued interest with respect to any such Security or portion thereof. On presentation and surrender of such Securities on or after the date fixed for redemption at the place of payment specified in the notice, said Securities shall be paid and redeemed at the applicable redemption price for such series, together with interest accrued thereon to the date fixed for redemption (but if the date fixed for redemption is an interest payment date, the interest installment payable on such date shall be payable to the registered holder at the close of business on the applicable record date pursuant to Section 2.03).

(2) Upon presentation of any Security of such series that is to be redeemed in part only, the Company shall execute and the Trustee shall authenticate and the office or agency where the Security is presented shall deliver to the holder thereof, at the expense of the Company, a new Security of the same series of authorized denominations in principal amount equal to the unredeemed portion of the Security so presented.

Section 3.04 Sinking Fund. The provisions of Sections 3.04, 3.05 and 3.06 shall be applicable to any sinking fund for the retirement of Securities of a series, except as otherwise specified as contemplated by Section 2.01 for Securities of such series.

The minimum amount of any sinking fund payment provided for by the terms of Securities of any series is herein referred to as a "mandatory sinking fund payment," and any payment in excess of such minimum amount provided for by the terms of Securities of any series is herein referred to as an "optional sinking fund payment". If provided for by the terms of Securities of any series, the cash amount of any sinking fund payment may be subject to reduction as provided in Section 3.05. Each sinking fund payment shall be applied to the redemption of Securities of any series as provided for by the terms of Securities of such series.

Section 3.05 Satisfaction of Sinking Fund Payments with Securities. The Company (i) may deliver Outstanding Securities of a series and (ii) may apply as a credit Securities of a series that have been redeemed either at the election of the Company pursuant to the terms of such Securities or through the application of permitted optional sinking fund payments pursuant to the terms of such Securities, in each case in satisfaction of all or any part of any sinking fund payment with respect to the Securities of such series required to be made pursuant to the terms of such Securities as provided for by the terms of such series, *provided* that such Securities have not been previously so credited. Such Securities shall be received and credited for such purpose by the Trustee at the redemption price specified in such Securities for redemption through operation of the sinking fund and the amount of such sinking fund payment shall be reduced accordingly.

Section 3.06 Redemption of Securities for Sinking Fund. Not less than 45 days prior to each sinking fund payment date for any series of Securities (unless a shorter period shall be satisfactory to the Trustee), the Company will deliver to the Trustee an Officer's Certificate specifying the amount of the next ensuing sinking fund payment for that series pursuant to the terms of the series, the portion thereof, if any, that is to be satisfied by delivering and crediting Securities of that series pursuant to Section 3.05 and the basis for such credit and will, together with such Officer's Certificate, deliver to the Trustee any Securities to be so delivered. Not less than 30 days before each such sinking fund payment date the Trustee shall select the Securities to be redeemed upon such sinking fund payment date in the manner specified in Section 3.02 and cause notice of the redemption thereof to be given in the name of and at the expense of the Company in the manner provided in Section 3.02. Such notice having been duly given, the redemption of such Securities shall be made upon the terms and in the manner stated in Section 3.03.

ARTICLE 4

COVENANTS

Section 4.01 Payment of Principal, Premium and Interest. The Company will duly and punctually pay or cause to be paid the principal of (and premium, if any) and interest on the Securities of that series at the time and place and in the manner provided herein and established with respect to such Securities. Payments of principal on the Securities may be made at the time provided herein and established with respect to such Securities by U.S. dollar check drawn on and mailed to the address of the Securityholder entitled thereto as such address shall appear in the Security Register, or U.S. dollar wire transfer to, a U.S. dollar account if such Securityholder shall have furnished wire instructions to the Trustee no later than 15 days prior to the relevant payment date. Payments of interest on the Securities may be made at the time provided herein and established with respect to such Securities by U.S. dollar check mailed to the address of the Securityholder entitled thereto as such address shall appear in the Security Register, or U.S. dollar wire transfer to, a U.S. dollar account if such Securityholder shall have furnished wire instructions in writing to the Security Registrar and the Trustee no later than 15 days prior to the relevant payment date.

Section 4.02 Maintenance of Office or Agency. So long as any series of the Securities remain Outstanding, the Company agrees to maintain an office or agency with respect to each such series and at such other location or locations as may be designated as provided in this Section 4.02, where (i) Securities of that series may be presented for payment, (ii) Securities of that series may be presented as herein above authorized for registration of transfer and exchange, and (iii) notices and demands to or upon the Company in respect of the Securities of that series and this Indenture may be given or served, such designation to continue with respect to such office or agency until the Company shall, by written notice signed by any officer authorized to sign an Officer's Certificate and delivered to the Trustee, designate some other office or agency for such purposes or any of them. If at any time the Company shall fail to maintain any such required office or agency or shall fail to furnish the Trustee with the address thereof, such presentations, notices and demands may be made or served at the Corporate Trust Office of the Trustee, and the Company hereby appoints the Trustee as its agent to receive all such presentations, notices and demands. The Company initially appoints the Corporate Trust Office of the Trustee as its paying agent with respect to the Securities.

Section 4.03 Paying Agents.

(1) If the Company shall appoint one or more paying agents for all or any series of the Securities, other than the Trustee, the Company will cause each such paying agent to execute and deliver to the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section:

(a) that it will hold all sums held by it as such agent for the payment of the principal of (and premium, if any) or interest on the Securities of that series (whether such sums have been paid to it by the Company or by any other obligor of such Securities) in trust for the benefit of the Persons entitled thereto;

(b) that it will give the Trustee notice of any failure by the Company (or by any other obligor of such Securities) to make any payment of the principal of (and premium, if any) or interest on the Securities of that series when the same shall be due and payable;

(c) that it will, at any time during the continuance of any failure referred to in the preceding paragraph (a)(2) above, upon the written request of the Trustee, forthwith pay to the Trustee all sums so held in trust by such paying agent; and

(d) that it will perform all other duties of paying agent as set forth in this Indenture.

(2) If the Company shall act as its own paying agent with respect to any series of the Securities, it will on or before each due date of the principal of (and premium, if any) or interest on Securities of that series, set aside, segregate and hold in trust for the benefit of the Persons entitled thereto a sum sufficient to pay such principal (and premium, if any) or interest so becoming due on Securities of that series until such sums shall be paid to such Persons or otherwise disposed of as herein provided and will promptly notify the Trustee of such action, or any failure (by it or any other obligor on such Securities) to take such action. Whenever the Company shall have one or more paying agents for any series of Securities, it will, prior to each due date of the principal of (and premium, if any) or interest on any Securities of that series, deposit with the paying agent a sum sufficient to pay the principal (and premium, if any) or interest so becoming due, such sum to be held in trust for the benefit of the Persons entitled to such principal, premium or interest, and (unless such paying agent is the Trustee) the Company will promptly notify the Trustee of this action or failure so to act.

(3) Notwithstanding anything in this Section to the contrary, (i) the agreement to hold sums in trust as provided in this Section is subject to the provisions of Section 11.05, and (ii) the Company may at any time, for the purpose of obtaining the satisfaction and discharge of this Indenture or for any other purpose, pay, or direct any paying agent to pay, to the Trustee all sums held in trust by the Company or such paying agent, such sums to be held by the Trustee upon the same terms and conditions as those upon which such sums were held by the Company or such paying agent; and, upon such payment by the Company or any paying agent to the Trustee, the Company or such paying agent shall be released from all further liability with respect to such money.

Section 4.04 Appointment to Fill Vacancy in Office of Trustee. The Company, whenever necessary to avoid or fill a vacancy in the office of Trustee, will appoint, in the manner provided in Section 7.10, a Trustee, so that there shall at all times be a Trustee hereunder.

Section 4.05 Compliance with Consolidation Provisions. The Company will not, while any of the Securities remain Outstanding, consolidate with or merge into any other Person, in either case where the Company is not the survivor of such transaction, or sell or convey all or substantially all of its property to any other Person unless the provisions of Article Ten hereof are complied with.

ARTICLE 5

SECURITYHOLDERS' LISTS AND REPORTS BY THE COMPANY AND THE TRUSTEE

Section 5.01 Company to Furnish Trustee Names and Addresses of Securityholders. The Company will furnish or cause to be furnished to the Trustee (a) within 15 days after each regular record date (as defined in Section 2.03) a list, in such form as the Trustee may reasonably require, of the names and addresses of the holders of each series of Securities as of such regular record date, *provided* that the Company shall not be obligated to furnish

or cause to furnish such list at any time that the list shall not differ in any respect from the most recent list furnished to the Trustee by the Company and (b) at such other times as the Trustee may request in writing within 30 days after the receipt by the Company of any such request, a list of similar form and content as of a date not more than 15 days prior to the time such list is furnished; *provided*, *however*, that, in either case, no such list need be furnished for any series for which the Trustee shall be the Security Registrar.

Section 5.02 Preservation Of Information; Communications With Securityholders.

(1) The Trustee shall preserve, in as current a form as is reasonably practicable, all information as to the names and addresses of the holders of Securities contained in the most recent list furnished to it as provided in Section 5.01 and as to the names and addresses of holders of Securities received by the Trustee in its capacity as Security Registrar (if acting in such capacity).

(2) The Trustee may destroy any list furnished to it as provided in Section 5.01 upon receipt of a new list so furnished.

(3) Securityholders may communicate as provided in Section 312(b) of the Trust Indenture Act with other Securityholders with respect to their rights under this Indenture or under the Securities, and, in connection with any such communications, the Trustee shall satisfy its obligations under Section 312(b) of the Trust Indenture Act in accordance with the provisions of Section 312(b) of the Trust Indenture Act.

Section 5.03 Reports by the Company.

(1) The Company covenants and agrees to provide (which delivery may be via electronic mail) to the Trustee within 30 days, after the Company files the same with the Commission, copies of the annual reports and of the information, documents and other reports (or copies of such portions of any of the foregoing as the Commission may from time to time by rules and regulations prescribe) that the Company is required to file with the Commission pursuant to Section 13 or Section 15(d) of the Exchange Act; *provided*, *however*, the Company shall not be required to deliver to the Trustee any materials for which the Company has sought and received confidential treatment by the Commission; and provided further, that so long as such filings by the Company are available on the Commission's Electronic Data Gathering, Analysis and Retrieval System (EDGAR), or Interactive Data Electronic Applications (IDEA), or any successor system, such filings shall be deemed to have been filed with the Trustee for purposes hereof without any further action required by the Company; *provided* that an electronic link to such filing, together with an electronic notice of such filing have been sent to the Trustee. For the avoidance of doubt, a failure by the Company to file annual reports, information and other reports with the SEC within the time period prescribed thereof by the Commission shall not be deemed a breach of this Section 5.03.

(2) Delivery of reports, information and documents to the Trustee under Section 5.03 is for informational purposes only and the information and the Trustee's receipt of the foregoing shall not constitute constructive notice of any information contained therein, or determinable from information contained therein including the Company's compliance with any of their covenants thereunder (as to which the Trustee is entitled to rely exclusively on an Officer's Certificate).

Section 5.04 Reports by the Trustee.

(1) If required by Section 313(a) of the Trust Indenture Act, the Trustee, within sixty (60) days after each May 1, shall transmit by mail, first class postage prepaid, to the Securityholders, as their names and addresses appear upon the Security Register, a brief report dated as of such May 1, which complies with Section 313(a) of the Trust Indenture Act.

(2) The Trustee shall comply with Section 313(b) and 313(c) of the Trust Indenture Act.

(3) A copy of each such report shall, at the time of such transmission to Securityholders, be filed by the Trustee with the Company, with each securities exchange upon which any Securities are listed (if so listed) and also with the Commission. The Company agrees to notify the Trustee when any Securities become listed on any securities exchange.

ARTICLE 6

REMEDIES OF THE TRUSTEE AND SECURITYHOLDERS ON EVENT OF DEFAULT

Section 6.01 Events of Default.

(1) Whenever used herein with respect to Securities of a particular series, "Event of Default" means any one or more of the following events that has occurred and is continuing:

(a) the Company defaults in the payment of any installment of interest upon any of the Securities of that series, as and when the same shall become due and payable, and such default continues for a period of 90 days; *provided, however*, that a valid extension of an interest payment period by the Company in accordance with the terms of any indenture supplemental hereto shall not constitute a default in the payment of interest for this purpose;

(b) the Company defaults in the payment of the principal of (or premium, if any, on) any of the Securities of that series as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to that series; *provided, however*, that a valid extension of the maturity of such Securities in accordance with the terms of any indenture supplemental hereto shall not constitute a default in the payment of principal or premium, if any;

(c) the Company fails to observe or perform any other of its covenants or agreements with respect to that series contained in this Indenture or otherwise established with respect to that series of Securities pursuant to Section 2.01 hereof (other than a covenant or agreement that has been expressly included in this Indenture solely for the benefit of one or more series of Securities other than such series) for a period of 90 days after the date on which written notice of such failure, requiring the same to be remedied and stating that such notice is a "Notice of Default" hereunder, shall have been given to the Company by the Trustee, by registered or certified mail, or to the Company and the Trustee by the holders of at least 25% in principal amount of the Securities of that series at the time Outstanding;

(d) the Company pursuant to or within the meaning of any Bankruptcy Law (i) commences a voluntary case, (ii) consents to the entry of an order for relief against it in an involuntary case, (iii) consents to the appointment of a Custodian of it or for all or substantially all of its property or (iv) makes a general assignment for the benefit of its creditors; or

(e) a court of competent jurisdiction enters an order under any Bankruptcy Law that (i) is for relief against the Company in an involuntary case, (ii) appoints a Custodian of the Company for all or substantially all of its property or (iii) orders the liquidation of the Company, and the order or decree remains unstayed and in effect for 90 days.

(2) In each and every such case (other than an Event of Default specified in clause (4) or clause (5) above), unless the principal of all the Securities of that series shall have already become due and payable, either the Trustee or the holders of not less than 25% in aggregate principal amount of the Securities of that series then Outstanding hereunder, by notice in writing to the Company (and to the Trustee if given by such Securityholders), may declare the principal of (and premium, if any, on) and accrued and unpaid interest on all the Securities of that series to be due and payable immediately, and upon any such declaration the same shall become and shall be immediately due and payable. If an Event of Default specified in clause (4) or clause (5) above occurs, the principal of and accrued and unpaid interest on all the Securities of that series shall automatically be immediately due and payable without any declaration or other act on the part of the Trustee or the holders of the Securities.

(3) At any time after the principal of (and premium, if any, on) and accrued and unpaid interest on the Securities of that series shall have been so declared due and payable, and before any judgment or decree for the payment of the moneys due shall have been obtained or entered as hereinafter provided, the holders of

a majority in aggregate principal amount of the Securities of that series then Outstanding hereunder, by written notice to the Company and the Trustee, may rescind and annul such declaration and its consequences if: (i) the Company has paid or deposited with the Trustee a sum sufficient to pay all matured installments of interest upon all the Securities of that series and the principal of (and premium, if any, on) any and all Securities of that series that shall have become due otherwise than by acceleration (with interest upon such principal and premium, if any, and, to the extent that such payment is enforceable under applicable law, upon overdue installments of interest, at the rate per annum expressed in the Securities of that series to the date of such payment or deposit) and the amount payable to the Trustee under Section 7.06, and (ii) any and all Events of Default under the Indenture with respect to such series, other than the nonpayment of principal on (and premium, if any, on) and accrued and unpaid interest on Securities of that series that shall not have become due by their terms, shall have been remedied or waived as provided in Section 6.06.

No such rescission and annulment shall extend to or shall affect any subsequent default or impair any right consequent thereon.

(4) In case the Trustee shall have proceeded to enforce any right with respect to Securities of that series under this Indenture and such proceedings shall have been discontinued or abandoned because of such rescission or annulment or for any other reason or shall have been determined adversely to the Trustee, then and in every such case, subject to any determination in such proceedings, the Company and the Trustee shall be restored respectively to their former positions and rights hereunder, and all rights, remedies and powers of the Company and the Trustee shall continue as though no such proceedings had been taken.

Section 6.02 Collection of Indebtedness and Suits for Enforcement by Trustee.

(1) The Company covenants that (i) in case it shall default in the payment of any installment of interest on any of the Securities of a series, or in any payment required by any sinking or analogous fund established with respect to that series as and when the same shall have become due and payable, and such default shall have continued for a period of 90 days, or (ii) in case it shall default in the payment of the principal of (or premium, if any, on) any of the Securities of a series when the same shall have become due and payable, whether upon maturity of the Securities of a series or upon redemption or upon declaration or otherwise then, upon demand of the Trustee, the Company will pay to the Trustee, for the benefit of the holders of the Securities of that series, the whole amount that then shall have been become due and payable on all such Securities for principal (and premium, if any) or interest, or both, as the case may be, with interest upon the overdue principal (and premium, if any) and (to the extent that payment of such interest is enforceable under applicable law) upon overdue installments of interest at the rate per annum expressed in the Securities of that series; and, in addition thereto, such further amount as shall be sufficient to cover the costs and expenses of collection, and the amount payable to the Trustee under Section 7.06.

(2) If the Company shall fail to pay such amounts forthwith upon such demand, the Trustee, in its own name and as trustee of an express trust, shall be entitled and empowered to institute any action or proceedings at law or in equity for the collection of the sums so due and unpaid, and may prosecute any such action or proceeding to judgment or final decree, and may enforce any such judgment or final decree against the Company or other obligor upon the Securities of that series and collect the moneys adjudged or decreed to be payable in the manner provided by law or equity out of the property of the Company or other obligor upon the Securities of that series, wherever situated.

(3) In case of any receivership, insolvency, liquidation, bankruptcy, reorganization, readjustment, arrangement, composition or judicial proceedings affecting the Company, or its creditors or property, the Trustee shall have power to intervene in such proceedings and take any action therein that may be permitted by the court and shall (except as may be otherwise provided by law) be entitled to file such proofs of claim and other papers and documents as may be necessary or advisable in order to have the claims of the Trustee and of the holders of Securities of such series allowed for the entire amount due and payable by the Company under the Indenture at the date of institution of such proceedings and for any additional amount that may become due and payable by the Company after such date, and to collect and receive any moneys or other property payable or deliverable on any such claim, and to distribute the same after the deduction of the amount payable to the Trustee under Section 7.06; and any receiver, assignee or trustee in bankruptcy or reorganization is hereby authorized by each of the holders of Securities of such series to make such payments to the Trustee, and, in the event that the Trustee shall consent to the making of such payments directly to such Securityholders, to pay to the Trustee any amount due it under Section 7.06.

(4) All rights of action and of asserting claims under this Indenture, or under any of the terms established with respect to Securities of that series, may be enforced by the Trustee without the possession of any of such Securities, or the production thereof at any trial or other proceeding relative thereto, and any such suit or proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for payment to the Trustee of any amounts due under Section 7.06, be for the ratable benefit of the holders of the Securities of such series.

In case of an Event of Default hereunder, the Trustee may in its discretion proceed to protect and enforce the rights vested in it by this Indenture by such appropriate judicial proceedings as the Trustee shall deem most effectual to protect and enforce any of such rights, either at law or in equity or in bankruptcy or otherwise, whether for the specific enforcement of any covenant or agreement contained in the Indenture or in aid of the exercise of any power granted in this Indenture, or to enforce any other legal or equitable right vested in the Trustee by this Indenture or by law.

Nothing contained herein shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Securityholder any plan of reorganization, arrangement, adjustment or composition affecting the Securities of that series or the rights of any holder thereof or to authorize the Trustee to vote in respect of the claim of any Securityholder in any such proceeding.

Section 6.03 Application of Moneys Collected. Any moneys collected by the Trustee pursuant to this Article with respect to a particular series of Securities shall be applied in the following order, at the date or dates fixed by the Trustee and, in case of the distribution of such moneys on account of principal (or premium, if any) or interest, upon presentation of the Securities of that series, and notation thereon of the payment, if only partially paid, and upon surrender thereof if fully paid:

FIRST: To the payment of all indebtedness of the Company to which such series of Securities is subordinated to the extent required by Section 7.06 and any subordination terms of the series specified as contemplated by Article Fourteen;

SECOND: To the payment of the amounts then due and unpaid upon Securities of such series for principal (and premium, if any) and interest, in respect of which or for the benefit of which such money has been collected, ratably, without preference or priority of any kind, according to the amounts due and payable on such Securities for principal (and premium, if any) and interest, respectively; and

THIRD: To the payment of the remainder, if any, to the Company or any other Person lawfully entitled thereto.

Section 6.04 Limitation on Suits. No holder of any Security of any series shall have any right by virtue or by availing of any provision of this Indenture or any Security to institute any suit, action or proceeding in equity or at law upon or under or with respect to this Indenture, any Security or for the appointment of a receiver or trustee, or for any other remedy hereunder, unless (i) such holder previously shall have given to the Trustee written notice of an Event of Default and of the continuance thereof with respect to the Securities of such series specifying such Event of Default, as hereinbefore provided; (ii) the holders of not less than 25% in aggregate principal amount of the Securities of such series then Outstanding shall have made written request upon the Trustee to institute such action, suit or proceeding in its own name as Trustee hereunder; (iii) such holder or holders shall have offered to the Trustee such reasonable indemnity as it may require against the costs, expenses and liabilities to be incurred therein or thereby; (iv) the Trustee for 90 days after its receipt of such notice, request and offer of indemnity, shall have failed to institute any such action, suit or proceeding and (v) during such 90 day period, the holders of a majority in principal amount of the Securities of that series do not give the Trustee a direction inconsistent with the request.

Notwithstanding anything contained herein to the contrary or any other provisions of this Indenture, the right of any holder of any Security to receive payment of the principal of (and premium, if any) and interest on such Security, as therein provided, on or after the respective due dates expressed in such Security (or in the case of

redemption, on the redemption date), or to institute suit for the enforcement of any such payment on or after such respective dates or redemption date, shall not be impaired or affected without the consent of such holder and by accepting a Security hereunder it is expressly understood, intended and covenanted by the taker and holder of every Security of such series with every other such taker and holder and the Trustee, that no one or more holders of Securities of such series shall have any right in any manner whatsoever by virtue or by availing of any provision of this Indenture to affect, disturb or prejudice the rights of the holders of any other of such Securities, or to obtain or seek to obtain priority over or preference to any other such holder, or to enforce any right under this Indenture, except in the manner herein provided and for the equal, ratable and common benefit of all holders of Securities of such series. For the protection and enforcement of the provisions of this Section, each and every Securityholder and the Trustee shall be entitled to such relief as can be given either at law or in equity.

Section 6.05 Rights and Remedies Cumulative; Delay or Omission Not Waiver.

(1) Except as otherwise provided in Section 2.07, all powers and remedies given by this Article to the Trustee or to the Securityholders shall, to the extent permitted by law, be deemed cumulative and not exclusive of any other powers and remedies available to the Trustee or the holders of the Securities, by judicial proceedings or otherwise, to enforce the performance or observance of the covenants and agreements contained in this Indenture or otherwise established with respect to such Securities.

(2) No delay or omission of the Trustee or of any holder of any of the Securities to exercise any right or power accruing upon any Event of Default occurring and continuing as aforesaid shall impair any such right or power, or shall be construed to be a waiver of any such default or an acquiescence therein; and, subject to the provisions of Section 6.04, every power and remedy given by this Article or by law to the Trustee or the Securityholders may be exercised from time to time, and as often as shall be deemed expedient, by the Trustee or by the Securityholders.

Section 6.06 Control by Securityholders. The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding, determined in accordance with Section 8.04, shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred on the Trustee with respect to such series; *provided*, *however*, that such direction shall not be in conflict with any rule of law or with this Indenture or subject the Trustee in its sole discretion to personal liability. Subject to the provisions of Section 7.01, the Trustee shall have the right to decline to follow any such direction if the Trustee in good faith shall, by a Responsible Officer or officers of the Trustee, determine that the proceeding so directed, subject to the Trustee's duties under the Trust Indenture Act, would involve the Trustee in personal liability or might be unduly prejudicial to the Securityholders not involved in the proceeding. The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding affected thereby, determined in accordance with Section 8.04, may on behalf of the holders of all of the Securities of such series waive any past default in the performance of any of the covenants contained herein or established pursuant to Section 2.01 with respect to such series and its consequences, except a default in the payment of the principal of, or premium, if any, or interest on, any of the Securities of that series as and when the same shall become due by the terms of such Securities otherwise than by acceleration (unless such default has been cured and a sum sufficient to pay all matured installments of interest and principal and any premium has been deposited with the Trustee (in accordance with Section 6.01(3)). Upon any such waiver, the default covered thereby shall be deemed to be cured for all purposes of this Indenture and the Company, the Trustee and the holders of the Securities of such series shall be restored to their former positions and rights hereunder, respectively; but no such waiver shall extend to any subsequent or other default or impair any right consequent thereon.

Section 6.07 Undertaking to Pay Costs. All parties to this Indenture agree, and each holder of any Securities by such holder's acceptance thereof shall be deemed to have agreed, that any court may in its discretion require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit, and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; but the provisions of this Section shall not apply to any suit instituted by the Trustee, to any suit instituted by any Securityholder, or group of Securityholders, holding more than 10% in aggregate principal amount of the Outstanding Securities of any series, or to any suit instituted by any Securityholder for the enforcement of the payment of the principal of (or premium, if any) or interest on any Security of such series, on or after the respective due dates expressed in such Security or established pursuant to this Indenture.

ARTICLE 7

CONCERNING THE TRUSTEE

Section 7.01 Certain Duties and Responsibilities of Trustee.

(1) The Trustee, prior to the occurrence of an Event of Default with respect to the Securities of a series and after the curing of all Events of Default with respect to the Securities of that series that may have occurred, shall undertake to perform with respect to the Securities of such series such duties and only such duties as are specifically set forth in this Indenture, and no implied covenants shall be read into this Indenture against the Trustee. In case an Event of Default with respect to the Securities of a series has occurred (that has not been cured or waived), the Trustee shall exercise with respect to Securities of that series such of the rights and powers vested in it by this Indenture, and use the same degree of care and skill in their exercise, as a prudent man would exercise or use under the circumstances in the conduct of his own affairs.

(2) No provision of this Indenture shall be construed to relieve the Trustee from liability for its own gross negligence, or its own willful misconduct, except that:

(a) prior to the occurrence of an Event of Default with respect to the Securities of a series and after the curing or waiving of all such Events of Default with respect to that series that may have occurred:

(A) the duties and obligations of the Trustee shall with respect to the Securities of such series be determined solely by the express provisions of this Indenture, and the Trustee shall not be liable with respect to the Securities of such series except for the performance of such duties and obligations as are specifically set forth in this Indenture, and no implied covenants or obligations shall be read into this Indenture against the Trustee; and

(B) in the absence of bad faith on the part of the Trustee, the Trustee may with respect to the Securities of such series conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture; but in the case of any such certificates or opinions that by any provision hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine in good faith whether or not, in the Trustee's reasonable judgment, they conform to the requirements of this Indenture;

(b) the Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer or Responsible Officers of the Trustee, unless it shall be proved that the Trustee was grossly negligent in ascertaining the pertinent facts;

(c) the Trustee shall not be liable with respect to any action taken or omitted to be taken by it in good faith in accordance with the direction of the holders of not less than a majority in principal amount of the Securities of any series at the time Outstanding relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee under this Indenture with respect to the Securities of that series; and

(d) none of the provisions contained in this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur personal financial liability in the performance of any of its duties or in the exercise of any of its rights or powers if there is reasonable ground for believing that the repayment of such funds or liability is not reasonably assured to it under the terms of this Indenture or adequate indemnity against such risk is not reasonably assured to it.

Section 7.02 Certain Rights of Trustee. Except as otherwise provided in Section 7.01:

(1) The Trustee may rely and shall be fully protected and indemnified in acting or refraining from acting upon any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, approval, bond, security or other paper or document believed by it to be genuine and to have been signed or presented by the proper party or parties;

(2) Any request, direction, order or demand of the Company mentioned herein shall be sufficiently evidenced by a Board Resolution or an instrument signed in the name of the Company by any authorized officer of the Company (unless other evidence in respect thereof is specifically prescribed herein);

(3) The Trustee may consult with counsel and the written advice of such counsel or, if requested, any Opinion of Counsel shall be full and complete authorization and protection in respect of any action taken or suffered or omitted hereunder in good faith and in reliance thereon;

(4) The Trustee shall be under no obligation to exercise any of the rights or powers vested in it by this Indenture at the request, order or direction of any of the Securityholders pursuant to the provisions of this Indenture, unless such Securityholders shall have offered to the Trustee reasonable security or indemnity against the costs, expenses and liabilities that may be incurred therein or thereby; nothing contained herein shall, however, relieve the Trustee of the obligation, upon the occurrence of an Event of Default with respect to a series of the Securities (that has not been cured or waived), to exercise with respect to Securities of that series such of the rights and powers vested in it by this Indenture, and to use the same degree of care and skill in their exercise, as a prudent man would exercise or use under the circumstances in the conduct of his own affairs;

(5) The Trustee shall not be liable for any action taken or omitted to be taken by it in good faith and believed by it to be authorized or within the discretion or rights or powers conferred upon it by this Indenture;

(6) The Trustee shall not be bound to make any investigation into the facts or matters stated in any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, approval, bond, security, or other papers or documents, unless requested in writing so to do by the holders of not less than a majority in principal amount of the Outstanding Securities of the particular series affected thereby (determined as provided in Section 8.04); *provided, however*, that if the payment within a reasonable time to the Trustee of the costs, expenses or liabilities likely to be incurred by it in the making of such investigation is, in the opinion of the Trustee, not reasonably assured to the Trustee by the security afforded to it by the terms of this Indenture, the Trustee may require reasonable indemnity against such costs, expenses or liabilities as a condition to so proceeding. The reasonable expense of every such examination shall be paid by the Company or, if paid by the Trustee, shall be repaid by the Company upon demand;

(7) The Trustee may execute any of the trusts or powers hereunder or perform any duties hereunder either directly or by or through agents or attorneys and the Trustee shall not be responsible for any misconduct or negligence on the part of any agent or attorney appointed with due care by it hereunder;

(8) In no event shall the Trustee be responsible or liable for any failure or delay in the performance of its obligations hereunder arising out of or caused by, directly or indirectly, forces beyond its control, including, without limitation, strikes, work stoppages, accidents, acts of war or terrorism, civil or military disturbances, nuclear or natural catastrophes or acts of God, and interruptions, loss or malfunctions of utilities, communications or computer (software and hardware) services; it being understood that the Trustee shall use reasonable efforts which are consistent with accepted practices in the banking industry to resume performance as soon as practicable under the circumstances;

(9) In no event shall the Trustee be responsible or liable for special, indirect, or consequential loss or damage of any kind whatsoever (including, but not limited to, loss of profit) irrespective of whether the Trustee has been advised of the likelihood of such loss or damage and regardless of the form of action; and

(10) The Trustee agrees to accept and act upon instructions or directions pursuant to this Indenture sent by unsecured e-mail, facsimile transmission or other similar unsecured electronic methods; *provided, however*, that (a) the party providing such written instructions, subsequent to such transmission of written instructions, shall provide the originally executed instructions or directions to the Trustee in a timely manner, and (b) such originally executed instructions or directions shall be signed by an authorized representative of the party providing such instructions or directions. If the party elects to give the Trustee e-mail or facsimile instructions (or instructions by a similar electronic method) and the Trustee in its discretion elects to act upon such instructions, the Trustee's understanding of such instructions shall be deemed controlling. The Trustee shall not be liable for any losses, costs or expenses arising directly or indirectly from the Trustee's reliance upon and compliance with such instructions notwithstanding such instructions conflict or are inconsistent with a subsequent written instruction. The party providing electronic instructions agrees to assume all risks arising out of the use of such electronic methods to submit instructions and directions to the Trustee, including without limitation the risk of the Trustee acting on unauthorized instructions, and the risk or interception and misuse by third parties.

In addition, the Trustee shall not be deemed to have knowledge of any Default or Event of Default until the Trustee shall have received written notification in the manner set forth in this Indenture or a Responsible Officer of the Trustee shall have obtained actual knowledge.

Section 7.03 Trustee Not Responsible for Recitals or Issuance or Securities.

(1) The recitals contained herein and in the Securities shall be taken as the statements of the Company, and the Trustee assumes no responsibility for the correctness of the same.

(2) The Trustee makes no representations as to the validity or sufficiency of this Indenture or of the Securities.

(3) The Trustee shall not be accountable for the use or application by the Company of any of the Securities or of the proceeds of such Securities, or for the use or application of any moneys paid over by the Trustee in accordance with any provision of this Indenture or established pursuant to Section 2.01, or for the use or application of any moneys received by any paying agent other than the Trustee.

Section 7.04 May Hold Securities. The Trustee or any paying agent or Security Registrar, in its individual or any other capacity, may become the owner or pledgee of Securities with the same rights it would have if it were not Trustee, paying agent or Security Registrar.

Section 7.05 Moneys Held in Trust. Subject to the provisions of Section 11.05, all moneys received by the Trustee shall, until used or applied as herein provided, be held in trust for the purposes for which they were received, but need not be segregated from other funds except to the extent required by law. The Trustee shall be under no liability for interest on any moneys received by it hereunder except such as it may agree with the Company to pay thereon.

Section 7.06 Compensation and Reimbursement.

(1) The Company covenants and agrees to pay to the Trustee, and the Trustee shall be entitled to, such reasonable compensation (which shall not be limited by any provision of law in regard to the compensation of a trustee of an express trust) as the Company and the Trustee may from time to time agree in writing, for all services rendered by it in the execution of the trusts hereby created and in the exercise and performance of any of the powers and duties hereunder of the Trustee, and, except as otherwise expressly provided herein, the Company will pay or reimburse the Trustee upon its request for all reasonable expenses, disbursements and advances incurred or made by the Trustee in accordance with any of the provisions of this Indenture (including the reasonable compensation and the expenses and disbursements of its counsel and of all Persons not regularly in its employ), except any such expense, disbursement or advance as may arise from its negligence or bad faith and except as the Company and Trustee may from time to time agree in writing. The Company also covenants to indemnify the Trustee (and its officers, agents, directors and employees) for, and to hold it harmless against, any loss, liability or expense incurred without gross negligence or bad faith on the part of the Trustee and arising out of or in connection with the acceptance or administration of this trust, including the reasonable costs and expenses of defending itself against any claim of liability in the premises.

(2) The obligations of the Company under this Section to compensate and indemnify the Trustee and to pay or reimburse the Trustee for reasonable expenses, disbursements and advances shall constitute indebtedness of the Company to which the Securities are subordinated. Such additional indebtedness shall be secured by a lien prior to that of the Securities upon all property and funds held or collected by the Trustee as such, except funds held in trust for the benefit of the holders of particular Securities.

(3) To ensure the Company's payment obligations in this Section, the Trustee shall have a lien prior to the Securities on all funds or property held or collected by the Trustee, except that held in trust to pay principal of or interest on particular Securities. When the Trustee incurs expenses or renders services in connection with an Event of Default specified in Section 6.01(1)(d) or (1)(e), the expenses (including the reasonable fees and expenses of its counsel) and the compensation for services in connection therewith are to constitute expenses of administration under any bankruptcy law. The provisions of this Section 7.06 shall survive the termination of this Indenture and the resignation or removal of the Trustee.

Section 7.07 Reliance on Officer's Certificate. Except as otherwise provided in Section 7.01, whenever in the administration of the provisions of this Indenture the Trustee shall deem it reasonably necessary or desirable that a matter be proved or established prior to taking or suffering or omitting to take any action hereunder, such matter (unless other evidence in respect thereof be herein specifically prescribed) may, in the absence of negligence or bad faith on the part of the Trustee, be deemed to be conclusively proved and established by an Officer's Certificate delivered to the Trustee and such certificate, in the absence of negligence or bad faith on the part of the Trustee, shall be full warrant to the Trustee for any action taken, suffered or omitted to be taken by it under the provisions of this Indenture upon the faith thereof.

Section 7.08 Disqualification; Conflicting Interests. If the Trustee has or shall acquire any "conflicting interest" within the meaning of Section 310(b) of the Trust Indenture Act, the Trustee and the Company shall in all respects comply with the provisions of Section 310(b) of the Trust Indenture Act.

Section 7.09 Corporate Trustee Required; Eligibility. There shall at all times be a Trustee with respect to the Securities issued hereunder which shall at all times be a corporation organized and doing business under the laws of the United States of America or any state or territory thereof or of the District of Columbia, or a corporation or other Person permitted to act as trustee by the Commission, authorized under such laws to exercise corporate trust powers, having a combined capital and surplus of at least fifty million U.S. dollars ($50,000,000), and subject to supervision or examination by federal, state, territorial, or District of Columbia authority.

If such corporation or other Person publishes reports of condition at least annually, pursuant to law or to the requirements of the aforesaid supervising or examining authority, then for the purposes of this Section, the combined capital and surplus of such corporation or other Person shall be deemed to be its combined capital and surplus as set forth in its most recent report of condition so published. The Company may not, nor may any Person directly or indirectly controlling, controlled by, or under common control with the Company, serve as Trustee. In case at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section, the Trustee shall resign immediately in the manner and with the effect specified in Section 7.10.

Section 7.10 Resignation and Removal; Appointment of Successor.

(1) The Trustee or any successor hereafter appointed may at any time resign with respect to the Securities of one or more series by giving written notice thereof to the Company and by transmitting notice of resignation by mail, first class postage prepaid, to the Securityholders of such series, as their names and addresses appear upon the Security Register. Upon receiving such notice of resignation, the Company shall promptly appoint a successor trustee with respect to Securities of such series by written instrument, in duplicate, executed by order of the Board of Directors, one copy of which instrument shall be delivered to the resigning Trustee and one copy to the successor trustee. If no successor trustee shall have been so appointed and have accepted appointment within 30 days after the mailing of such notice of resignation, the resigning Trustee may petition any court of competent jurisdiction for the appointment of a successor trustee with respect to Securities of such series, or any

Securityholder of that series who has been a bona fide holder of a Security or Securities for at least six months may on behalf of himself and all others similarly situated, petition any such court for the appointment of a successor trustee. Such court may thereupon after such notice, if any, as it may deem proper and prescribe, appoint a successor trustee.

(2) In case at any time any one of the following shall occur:

(a) the Trustee shall fail to comply with the provisions of Section 7.08 after written request therefor by the Company or by any Securityholder who has been a bona fide holder of a Security or Securities for at least six months; or

(b) the Trustee shall cease to be eligible in accordance with the provisions of Section 7.09 and shall fail to resign after written request therefor by the Company or by any such Securityholder; or

(c) the Trustee shall become incapable of acting, or shall be adjudged a bankrupt or insolvent, or commence a voluntary bankruptcy proceeding, or a receiver of the Trustee or of its property shall be appointed or consented to, or any public officer shall take charge or control of the Trustee or of its property or affairs for the purpose of rehabilitation, conservation or liquidation;

then, in any such case, the Company may remove the Trustee with respect to all Securities and appoint a successor trustee by written instrument, in duplicate, executed by order of the Board of Directors, one copy of which instrument shall be delivered to the Trustee so removed and one copy to the successor trustee, or any Securityholder who has been a bona fide holder of a Security or Securities for at least six months may, on behalf of that holder and all others similarly situated, petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor trustee. Such court may thereupon after such notice, if any, as it may deem proper and prescribe, remove the Trustee and appoint a successor trustee.

(3) The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding may at any time remove the Trustee with respect to such series by so notifying the Trustee and the Company and may appoint a successor Trustee for such series with the consent of the Company.

(4) Any resignation or removal of the Trustee and appointment of a successor trustee with respect to the Securities of a series pursuant to any of the provisions of this Section shall become effective upon acceptance of appointment by the successor trustee as provided in Section 7.11.

(5) Any successor trustee appointed pursuant to this Section may be appointed with respect to the Securities of one or more series or all of such series, and at any time there shall be only one Trustee with respect to the Securities of any particular series.

Section 7.11 Acceptance of Appointment By Successor.

(1) In case of the appointment hereunder of a successor trustee with respect to all Securities, every such successor trustee so appointed shall execute, acknowledge and deliver to the Company and to the retiring Trustee an instrument accepting such appointment, and thereupon the resignation or removal of the retiring Trustee shall become effective and such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, trusts and duties of the retiring Trustee; but, on the request of the Company or the successor trustee, such retiring Trustee shall, upon payment of its charges, execute and deliver an instrument transferring to such successor trustee all the rights, powers, and trusts of the retiring Trustee and shall duly assign, transfer and deliver to such successor trustee all property and money held by such retiring Trustee hereunder.

(2) In case of the appointment hereunder of a successor trustee with respect to the Securities of one or more (but not all) series, the Company, the retiring Trustee and each successor trustee with respect to the Securities of one or more series shall execute and deliver an indenture supplemental hereto wherein each successor trustee shall accept such appointment and which (i) shall contain such provisions as shall be necessary or desirable to transfer and confirm to, and to vest in, each successor trustee all the rights, powers, trusts and duties of the retiring

Trustee with respect to the Securities of that or those series to which the appointment of such successor trustee relates, (ii) shall contain such provisions as shall be deemed necessary or desirable to confirm that all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series as to which the retiring Trustee is not retiring shall continue to be vested in the retiring Trustee, and (iii) shall add to or change any of the provisions of this Indenture as shall be necessary to provide for or facilitate the administration of the trusts hereunder by more than one Trustee, it being understood that nothing herein or in such supplemental indenture shall constitute such Trustees co-trustees of the same trust, that each such Trustee shall be trustee of a trust or trusts hereunder separate and apart from any trust or trusts hereunder administered by any other such Trustee and that no Trustee shall be responsible for any act or failure to act on the part of any other Trustee hereunder; and upon the execution and delivery of such supplemental indenture the resignation or removal of the retiring Trustee shall become effective to the extent provided therein, such retiring Trustee shall with respect to the Securities of that or those series to which the appointment of such successor trustee relates have no further responsibility for the exercise of rights and powers or for the performance of the duties and obligations vested in the Trustee under this Indenture, and each such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series to which the appointment of such successor trustee relates; but, on request of the Company or any successor trustee, such retiring Trustee shall duly assign, transfer and deliver to such successor trustee, to the extent contemplated by such supplemental indenture, the property and money held by such retiring Trustee hereunder with respect to the Securities of that or those series to which the appointment of such successor trustee relates.

(3) Upon request of any such successor trustee, the Company shall execute any and all instruments for more fully and certainly vesting in and confirming to such successor trustee all such rights, powers and trusts referred to in paragraph (a) or (b) of this Section, as the case may be.

(4) No successor trustee shall accept its appointment unless at the time of such acceptance such successor trustee shall be qualified and eligible under this Article.

(5) Upon acceptance of appointment by a successor trustee as provided in this Section, the Company shall transmit notice of the succession of such trustee hereunder by mail, first class postage prepaid, to the Securityholders, as their names and addresses appear upon the Security Register. If the Company fails to transmit such notice within ten days after acceptance of appointment by the successor trustee, the successor trustee shall cause such notice to be transmitted at the expense of the Company.

Section 7.12 Merger, Conversion, Consolidation or Succession to Business. Any corporation into which the Trustee may be merged or converted or with which it may be consolidated, or any corporation resulting from any merger, conversion or consolidation to which the Trustee shall be a party, or any corporation succeeding to the corporate trust business of the Trustee, including the administration of the trust created by this Indenture, shall be the successor of the Trustee hereunder, *provided* that such corporation shall be qualified under the provisions of Section 7.08 and eligible under the provisions of Section 7.09, without the execution or filing of any paper or any further act on the part of any of the parties hereto, anything herein to the contrary notwithstanding. In case any Securities shall have been authenticated, but not delivered, by the Trustee then in office, any successor by merger, conversion or consolidation to such authenticating Trustee may adopt such authentication and deliver the Securities so authenticated with the same effect as if such successor Trustee had itself authenticated such Securities.

Section 7.13 Preferential Collection of Claims Against the Company. The Trustee shall comply with Section 311(a) of the Trust Indenture Act, excluding any creditor relationship described in Section 311(b) of the Trust Indenture Act. A Trustee who has resigned or been removed shall be subject to Section 311(a) of the Trust Indenture Act to the extent included therein.

Section 7.14 Notice of Default. If any Event of Default occurs and is continuing and if such Event of Default is known to a Responsible Officer of the Trustee, the Trustee shall mail to each Securityholder in the manner and to the extent provided in Section 313(c) of the Trust Indenture Act notice of the Event of Default within the earlier of 90 days after it occurs and 30 days after it is known to a Responsible Officer of the Trustee or written notice of it is received by the Trustee, unless such Event of Default has been cured; *provided*, *however*, that, except in the case of a default in the payment of the principal of (or premium, if any) or interest on any Security, the Trustee shall be protected in withholding such notice if and so long as the board of directors, the executive committee or a trust committee of directors and/or Responsible Officers of the Trustee in good faith determine that the withholding of such notice is in the interest of the Securityholders.

ARTICLE 8

CONCERNING THE SECURITYHOLDERS

Section 8.01 Evidence of Action by Securityholders. Whenever in this Indenture it is provided that the holders of a majority or specified percentage in aggregate principal amount of the Securities of a particular series may take any action (including the making of any demand or request, the giving of any notice, consent or waiver or the taking of any other action), the fact that at the time of taking any such action the holders of such majority or specified percentage of that series have joined therein may be evidenced by any instrument or any number of instruments of similar tenor executed by such holders of Securities of that series in person or by agent or proxy appointed in writing.

If the Company shall solicit from the Securityholders of any series any request, demand, authorization, direction, notice, consent, waiver or other action, the Company may, at its option, as evidenced by an Officer's Certificate, fix in advance a record date for such series for the determination of Securityholders entitled to give such request, demand, authorization, direction, notice, consent, waiver or other action, but the Company shall have no obligation to do so. If such a record date is fixed, such request, demand, authorization, direction, notice, consent, waiver or other action may be given before or after the record date, but only the Securityholders of record at the close of business on the record date shall be deemed to be Securityholders for the purposes of determining whether Securityholders of the requisite proportion of Outstanding Securities of that series have authorized or agreed or consented to such request, demand, authorization, direction, notice, consent, waiver or other action, and for that purpose the Outstanding Securities of that series shall be computed as of the record date; *provided, however*, that no such authorization, agreement or consent by such Securityholders on the record date shall be deemed effective unless it shall become effective pursuant to the provisions of this Indenture not later than six months after the record date.

Section 8.02 Proof of Execution by Securityholders. Subject to the provisions of Section 7.01, proof of the execution of any instrument by a Securityholder (such proof will not require notarization) or his agent or proxy and proof of the holding by any Person of any of the Securities shall be sufficient if made in the following manner:

(1) The fact and date of the execution by any such Person of any instrument may be proved in any reasonable manner acceptable to the Trustee.

(2) The ownership of Securities shall be proved by the Security Register of such Securities or by a certificate of the Security Registrar thereof.

The Trustee may require such additional proof of any matter referred to in this Section as it shall deem necessary.

Section 8.03 Who May be Deemed Owners. Prior to the due presentment for registration of transfer of any Security, the Company, the Trustee, any paying agent and any Security Registrar may deem and treat the Person in whose name such Security shall be registered upon the books of the Company as the absolute owner of such Security (whether or not such Security shall be overdue and notwithstanding any notice of ownership or writing thereon made by anyone other than the Security Registrar) for the purpose of receiving payment of or on account of the principal of, premium, if any, and (subject to Section 2.03) interest on such Security and for all other purposes; and neither the Company nor the Trustee nor any paying agent nor any Security Registrar shall be affected by any notice to the contrary.

Section 8.04 Certain Securities Owned by Company Disregarded. In determining whether the holders of the requisite aggregate principal amount of Securities of a particular series have concurred in any direction, consent or waiver under this Indenture, the Securities of that series that are owned by the Company or any other obligor on the Securities of that series or by any Person directly or indirectly controlling or controlled by or under

common control with the Company or any other obligor on the Securities of that series shall be disregarded and deemed not to be Outstanding for the purpose of any such determination, except that for the purpose of determining whether the Trustee shall be protected in relying on any such direction, consent or waiver, only Securities of such series that the Trustee actually knows are so owned shall be so disregarded. The Securities so owned that have been pledged in good faith may be regarded as Outstanding for the purposes of this Section, if the pledgee shall establish to the satisfaction of the Trustee the pledgee's right so to act with respect to such Securities and that the pledgee is not a Person directly or indirectly controlling or controlled by or under direct or indirect common control with the Company or any such other obligor. In case of a dispute as to such right, any decision by the Trustee taken upon the advice of counsel shall be full protection to the Trustee.

Section 8.05 Actions Binding on Future Securityholders. At any time prior to (but not after) the evidencing to the Trustee, as provided in Section 8.01, of the taking of any action by the holders of the majority or percentage in aggregate principal amount of the Securities of a particular series specified in this Indenture in connection with such action, any holder of a Security of that series that is shown by the evidence to be included in the Securities the holders of which have consented to such action may, by filing written notice with the Trustee, and upon proof of holding as provided in Section 8.02, revoke such action so far as concerns such Security. Except as aforesaid any such action taken by the holder of any Security shall be conclusive and binding upon such holder and upon all future holders and owners of such Security, and of any Security issued in exchange therefor, on registration of transfer thereof or in place thereof, irrespective of whether or not any notation in regard thereto is made upon such Security. Any action taken by the holders of the majority or percentage in aggregate principal amount of the Securities of a particular series specified in this Indenture in connection with such action shall be conclusively binding upon the Company, the Trustee and the holders of all the Securities of that series.

ARTICLE 9

SUPPLEMENTAL INDENTURES

Section 9.01 Supplemental Indentures Without the Consent of Securityholders. In addition to any supplemental indenture otherwise authorized by this Indenture, the Company and the Trustee may from time to time and at any time enter into an indenture or indentures supplemental hereto (which shall conform to the provisions of the Trust Indenture Act as then in effect), without the consent of the Securityholders, for one or more of the following purposes:

(1) to cure any ambiguity, defect, or inconsistency herein or in the Securities of any series;

(2) to comply with Article Ten;

(3) to provide for uncertificated Securities in addition to or in place of certificated Securities;

(4) to add to the covenants, restrictions, conditions or provisions relating to the Company for the benefit of the holders of all or any series of Securities (and if such covenants, restrictions, conditions or provisions are to be for the benefit of less than all series of Securities, stating that such covenants, restrictions, conditions or provisions are expressly being included solely for the benefit of such series), to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an Event of Default, or to surrender any right or power herein conferred upon the Company;

(5) to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication, and delivery of Securities, as herein set forth;

(6) to make any change that does not adversely affect the rights of any Securityholder in any material respect;

(7) to provide for the issuance of and establish the form and terms and conditions of the Securities of any series as provided in Section 2.01, to establish the form of any certifications required to be furnished pursuant to the terms of this Indenture or any series of Securities, or to add to the rights of the holders of any series of Securities;

(8) to evidence and provide for the acceptance of appointment hereunder by a successor trustee; or

(9) to comply with any requirements of the Commission or any successor in connection with the qualification of this Indenture under the Trust Indenture Act.

The Trustee is hereby authorized to join with the Company in the execution of any such supplemental indenture, and to make any further appropriate agreements and stipulations that may be therein contained, but the Trustee shall not be obligated to enter into any such supplemental indenture that affects the Trustee's own rights, duties or immunities under this Indenture or otherwise.

Any supplemental indenture authorized by the provisions of this Section may be executed by the Company and the Trustee without the consent of the holders of any of the Securities at the time Outstanding, notwithstanding any of the provisions of Section 9.02.

Section 9.02 Supplemental Indentures With Consent of Securityholders. With the consent (evidenced as provided in Section 8.01) of the holders of not less than a majority in aggregate principal amount of the Securities of each series affected by such supplemental indenture or indentures at the time Outstanding, the Company, when authorized by a Board Resolution, and the Trustee may from time to time and at any time enter into an indenture or indentures supplemental hereto (which shall conform to the provisions of the Trust Indenture Act as then in effect) for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture or of any supplemental indenture or of modifying in any manner not covered by Section 9.01 the rights of the holders of the Securities of such series under this Indenture; *provided, however*, that no such supplemental indenture shall, without the consent of the holders of each Security then Outstanding and affected thereby, (a) extend the fixed maturity of any Securities of any series, or reduce the principal amount thereof, or reduce the rate or extend the time of payment of interest thereon, or reduce any premium payable upon the redemption thereof or (b) reduce the aforesaid percentage of Securities, the holders of which are required to consent to any such supplemental indenture.

It shall not be necessary for the consent of the Securityholders of any series affected thereby under this Section to approve the particular form of any proposed supplemental indenture, but it shall be sufficient if such consent shall approve the substance thereof.

Section 9.03 Effect of Supplemental Indentures. Upon the execution of any supplemental indenture pursuant to the provisions of this Article or of Section 10.01, this Indenture shall, with respect to such series, be and be deemed to be modified and amended in accordance therewith and the respective rights, limitations of rights, obligations, duties and immunities under this Indenture of the Trustee, the Company and the holders of Securities of the series affected thereby shall thereafter be determined, exercised and enforced hereunder subject in all respects to such modifications and amendments, and all the terms and conditions of any such supplemental indenture shall be and be deemed to be part of the terms and conditions of this Indenture for any and all purposes.

Section 9.04 Securities Affected by Supplemental Indentures. Securities of any series affected by a supplemental indenture, authenticated and delivered after the execution of such supplemental indenture pursuant to the provisions of this Article or of Section 10.01, may bear a notation in form approved by the Company, *provided* such form meets the requirements of any securities exchange upon which such series may be listed, as to any matter provided for in such supplemental indenture. If the Company shall so determine, new Securities of that series so modified as to conform, in the opinion of the Board of Directors, to any modification of this Indenture contained in any such supplemental indenture may be prepared by the Company, authenticated by the Trustee and delivered in exchange for the Securities of that series then Outstanding.

Section 9.05 Execution of Supplemental Indentures. Upon the request of the Company, accompanied by its Board Resolutions authorizing the execution of any such supplemental indenture, and upon the filing with the Trustee of evidence of the consent of Securityholders required to consent thereto as aforesaid, the Trustee shall join with the Company in the execution of such supplemental indenture unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture or otherwise, in which case the Trustee may in its

discretion but shall not be obligated to enter into such supplemental indenture. The Trustee, subject to the provisions of Section 7.01, shall receive an Officer's Certificate or an Opinion of Counsel as conclusive evidence that any supplemental indenture executed pursuant to this Article is authorized or permitted by the terms of this Article and that all conditions precedent to the execution of the supplemental indenture have been complied with; *provided, however*, that such Officer's Certificate or Opinion of Counsel need not be provided in connection with the execution of a supplemental indenture that establishes the terms of a series of Securities pursuant to Section 2.01 hereof.

Promptly after the execution by the Company and the Trustee of any supplemental indenture pursuant to the provisions of this Section, the Company shall (or shall direct the Trustee to) transmit by mail, first class postage prepaid, a notice, setting forth in general terms the substance of such supplemental indenture, to the Securityholders of all series affected thereby as their names and addresses appear upon the Security Register. Any failure of the Company to mail, or cause the mailing of, such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such supplemental indenture.

ARTICLE 10

SUCCESSOR ENTITY

Section 10.01 Company May Consolidate, Etc. Nothing contained in this Indenture shall prevent any consolidation or merger of the Company with or into any other Person (whether or not affiliated with the Company) or successive consolidations or mergers in which the Company or its successor or successors shall be a party or parties, or shall prevent any sale, conveyance, transfer or other disposition of the property of the Company or its successor or successors as an entirety, or substantially as an entirety, to any other corporation (whether or not affiliated with the Company or its successor or successors) authorized to acquire and operate the same; *provided, however*, (a) the Company hereby covenants and agrees that, upon any such consolidation or merger (in each case, if the Company is not the survivor of such transaction), sale, conveyance, transfer or other disposition, the due and punctual payment of the principal of (premium, if any) and interest on all of the Securities of all series in accordance with the terms of each series, according to their tenor, and the due and punctual performance and observance of all the covenants and conditions of this Indenture with respect to each series or established with respect to such series pursuant to Section 2.01 to be kept or performed by the Company shall be expressly assumed, by supplemental indenture (which shall conform to the provisions of the Trust Indenture Act, as then in effect) reasonably satisfactory in form to the Trustee executed and delivered to the Trustee by the entity formed by such consolidation, or into which the Company shall have been merged, or by the entity which shall have acquired such property and (b) in the event that the Securities of any series then Outstanding are convertible into or exchangeable for shares of common stock or other securities of the Company, such entity shall, by such supplemental indenture, make provision so that the Securityholders of Securities of that series shall thereafter be entitled to receive upon conversion or exchange of such Securities the number of securities or property to which a holder of the number of shares of common stock or other securities of the Company deliverable upon conversion or exchange of those Securities would have been entitled had such conversion or exchange occurred immediately prior to such consolidation, merger, sale, conveyance, transfer or other disposition.

Section 10.02 Successor Entity Substituted.

(1) In case of any such consolidation, merger, sale, conveyance, transfer or other disposition and upon the assumption by the successor entity by supplemental indenture, executed and delivered to the Trustee and satisfactory in form to the Trustee, of the obligations set forth under Section 10.01 on all of the Securities of all series Outstanding, such successor entity shall succeed to and be substituted for the Company with the same effect as if it had been named as the Company herein, and thereupon the predecessor corporation shall be relieved of all obligations and covenants under this Indenture and the Securities.

(2) In case of any such consolidation, merger, sale, conveyance, transfer or other disposition, such changes in phraseology and form (but not in substance) may be made in the Securities thereafter to be issued as may be appropriate.

(3) Nothing contained in this Article shall require any action by the Company in the case of a consolidation or merger of any Person into the Company where the Company is the survivor of such transaction, or the acquisition by the Company, by purchase or otherwise, of all or any part of the property of any other Person (whether or not affiliated with the Company).

ARTICLE 11

SATISFACTION AND DISCHARGE

Section 11.01 Satisfaction and Discharge of Indenture. If at any time: (a) the Company shall have delivered to the Trustee for cancellation all Securities of a series theretofore authenticated and not delivered to the Trustee for cancellation (other than any Securities that shall have been destroyed, lost or stolen and that shall have been replaced or paid as provided in Section 2.07 and Securities for whose payment money or Governmental Obligations have theretofore been deposited in trust or segregated and held in trust by the Company and thereupon repaid to the Company or discharged from such trust, as provided in Section 11.05); or (b) all such Securities of a particular series not theretofore delivered to the Trustee for cancellation shall have become due and payable, or are by their terms to become due and payable within one year or are to be called for redemption within one year under arrangements satisfactory to the Trustee for the giving of notice of redemption, and the Company shall deposit or cause to be deposited with the Trustee as trust funds the entire amount in moneys or Governmental Obligations or a combination thereof, sufficient in the opinion of a nationally recognized firm of independent public accountants expressed in a written certification thereof delivered to the Trustee, to pay at maturity or upon redemption all Securities of that series not theretofore delivered to the Trustee for cancellation, including principal (and premium, if any) and interest due or to become due to such date of maturity or date fixed for redemption, as the case may be, and if the Company shall also pay or cause to be paid all other sums payable hereunder with respect to such series by the Company then this Indenture shall thereupon cease to be of further effect with respect to such series except for the provisions of Sections 2.03, 2.05, 2.07, 4.01, 4.02, 4.03 and 7.10, that shall survive until the date of maturity or redemption date, as the case may be, and Sections 7.06 and 11.05, that shall survive to such date and thereafter, and the Trustee, on demand of the Company and at the cost and expense of the Company shall execute proper instruments acknowledging satisfaction of and discharging this Indenture with respect to such series.

Section 11.02 Discharge of Obligations. If at any time all such Securities of a particular series not heretofore delivered to the Trustee for cancellation or that have not become due and payable as described in Section 11.01 shall have been paid by the Company by depositing irrevocably with the Trustee as trust funds moneys or an amount of Governmental Obligations sufficient to pay at maturity or upon redemption all such Securities of that series not theretofore delivered to the Trustee for cancellation, including principal (and premium, if any) and interest due or to become due to such date of maturity or date fixed for redemption, as the case may be, and if the Company shall also pay or cause to be paid all other sums payable hereunder by the Company with respect to such series, then after the date such moneys or Governmental Obligations, as the case may be, are deposited with the Trustee the obligations of the Company under this Indenture with respect to such series shall cease to be of further effect except for the provisions of Sections 2.03, 2.05, 2.07, 4.01, 4.02, 4.03, 7.06, 7.10 and 11.05 hereof that shall survive until such Securities shall mature and be paid.

Thereafter, Sections 7.06 and 11.05 shall survive.

Section 11.03 Deposited Moneys to be Held in Trust. All moneys or Governmental Obligations deposited with the Trustee pursuant to Sections 11.01 or 11.02 shall be held in trust and shall be available for payment as due, either directly or through any paying agent (including the Company acting as its own paying agent), to the holders of the particular series of Securities for the payment or redemption of which such moneys or Governmental Obligations have been deposited with the Trustee.

Section 11.04 Payment of Moneys Held by Paying Agents. In connection with the satisfaction and discharge of this Indenture all moneys or Governmental Obligations then held by any paying agent under the provisions of this Indenture shall, upon demand of the Company, be paid to the Trustee and thereupon such paying agent shall be released from all further liability with respect to such moneys or Governmental Obligations.

Section 11.05 Repayment to Company. Any moneys or Governmental Obligations deposited with any paying agent or the Trustee, or then held by the Company, in trust for payment of principal of or premium, if any, or interest on the Securities of a particular series that are not applied but remain unclaimed by the holders of such Securities for at least two years after the date upon which the principal of (and premium, if any) or interest on such Securities shall have respectively become due and payable, or such other shorter period set forth in applicable escheat or abandoned or unclaimed property law, shall be repaid to the Company on May 31 of each year or upon the Company's request or (if then held by the Company) shall be discharged from such trust; and thereupon the paying agent and the Trustee shall be released from all further liability with respect to such moneys or Governmental Obligations, and the holder of any of the Securities entitled to receive such payment shall thereafter, as a general creditor, look only to the Company for the payment thereof.

ARTICLE 12

IMMUNITY OF INCORPORATORS, STOCKHOLDERS, OFFICERS AND DIRECTORS

Section 12.01 No Recourse. No recourse under or upon any obligation, covenant or agreement of this Indenture, or of any Security, or for any claim based thereon or otherwise in respect thereof, shall be had against any incorporator, stockholder, officer or director, past, present or future as such, of the Company or of any predecessor or successor corporation, either directly or through the Company or any such predecessor or successor corporation, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise; it being expressly understood that this Indenture and the obligations issued hereunder are solely corporate obligations, and that no such personal liability whatever shall attach to, or is or shall be incurred by, the incorporators, stockholders, officers or directors as such, of the Company or of any predecessor or successor corporation, or any of them, because of the creation of the indebtedness hereby authorized, or under or by reason of the obligations, covenants or agreements contained in this Indenture or in any of the Securities or implied therefrom; and that any and all such personal liability of every name and nature, either at common law or in equity or by constitution or statute, of, and any and all such rights and claims against, every such incorporator, stockholder, officer or director as such, because of the creation of the indebtedness hereby authorized, or under or by reason of the obligations, covenants or agreements contained in this Indenture or in any of the Securities or implied therefrom, are hereby expressly waived and released as a condition of, and as a consideration for, the execution of this Indenture and the issuance of such Securities.

ARTICLE 13

MISCELLANEOUS PROVISIONS

Section 13.01 Effect on Successors and Assigns. All the covenants, stipulations, promises and agreements in this Indenture made by or on behalf of the Company shall bind its successors and assigns, whether so expressed or not.

Section 13.02 Actions by Successor. Any act or proceeding by any provision of this Indenture authorized or required to be done or performed by any board, committee or officer of the Company shall and may be done and performed with like force and effect by the corresponding board, committee or officer of any corporation that shall at the time be the lawful successor of the Company.

Section 13.03 Surrender of Company Powers. The Company by instrument in writing executed by authority of its Board of Directors and delivered to the Trustee may surrender any of the powers reserved to the Company, and thereupon such power so surrendered shall terminate both as to the Company and as to any successor corporation.

Section 13.04 Notices. Except as otherwise expressly provided herein, any notice, request or demand that by any provision of this Indenture is required or permitted to be given, made or served by the Trustee or by the holders of Securities or by any other Person pursuant to this Indenture to or on the Company may be given or served by being deposited in first class mail, postage prepaid, addressed (until another address is filed in writing by the Company with the Trustee), as follows: . Any notice, election, request or demand by the Company or any Securityholder or by any other Person pursuant to this Indenture to or upon the Trustee shall be deemed to have been sufficiently given or made, for all purposes, if given or made in writing at the Corporate Trust Office of the Trustee.

Section 13.05 Governing Law. This Indenture and each Security shall be deemed to be a contract made under the internal laws of the State of New York, and for all purposes shall be construed in accordance with the laws of said State, except to the extent that the Trust Indenture Act is applicable.

Section 13.06 Treatment of Securities as Debt. It is intended that the Securities will be treated as indebtedness and not as equity for federal income tax purposes. The provisions of this Indenture shall be interpreted to further this intention.

Section 13.07 Certificates and Opinions as to Conditions Precedent.

(1) Upon any application or demand by the Company to the Trustee to take any action under any of the provisions of this Indenture, the Company shall furnish to the Trustee an Officer's Certificate stating that all conditions precedent provided for in this Indenture (other than the certificate to be delivered pursuant to Section 13.12) relating to the proposed action have been complied with and, if requested, an Opinion of Counsel stating that in the opinion of such counsel all such conditions precedent have been complied with, except that in the case of any such application or demand as to which the furnishing of such documents is specifically required by any provision of this Indenture relating to such particular application or demand, no additional certificate or opinion need be furnished.

(2) Each certificate or opinion provided for in this Indenture and delivered to the Trustee with respect to compliance with a condition or covenant in this Indenture shall include (i) a statement that the Person making such certificate or opinion has read such covenant or condition; (ii) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained in such certificate or opinion are based; (iii) a statement that, in the opinion of such Person, he has made such examination or investigation as is reasonably necessary to enable him to express an informed opinion as to whether or not such covenant or condition has been complied with; and (iv) a statement as to whether or not, in the opinion of such Person, such condition or covenant has been complied with.

Section 13.08 Payments on Business Days. Except as provided pursuant to Section 2.01 pursuant to a Board Resolution, and set forth in an Officer's Certificate, or established in one or more indentures supplemental to this Indenture, in any case where the date of maturity of interest or principal of any Security or the date of redemption of any Security shall not be a Business Day, then payment of interest or principal (and premium, if any) may be made on the next succeeding Business Day with the same force and effect as if made on the nominal date of maturity or redemption, and no interest shall accrue for the period after such nominal date.

Section 13.09 Conflict with Trust Indenture Act. If and to the extent that any provision of this Indenture limits, qualifies or conflicts with the duties imposed by Sections 310 to 317, inclusive, of the Trust Indenture Act, such imposed duties shall control.

Section 13.10 Counterparts. This Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument.

Section 13.11 Separability. In case any one or more of the provisions contained in this Indenture or in the Securities of any series shall for any reason be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other provisions of this Indenture or of such Securities, but this Indenture and such Securities shall be construed as if such invalid or illegal or unenforceable provision had never been contained herein or therein.

Section 13.12 Compliance Certificates. The Company shall deliver to the Trustee, within 120 days after the end of each fiscal year during which any Securities of any series were outstanding, an officer's certificate stating whether or not the signers know of any Event of Default that occurred during such fiscal year. Such certificate shall contain a certification from the principal executive officer, principal financial officer or principal accounting officer of the Company that a review has been conducted of the activities of the Company and the Company's performance

under this Indenture and that the Company has complied with all conditions and covenants under this Indenture. For purposes of this Section 13.12, such compliance shall be determined without regard to any period of grace or requirement of notice provided under this Indenture. If the officer of the Company signing such certificate has knowledge of such an Event of Default, the certificate shall describe any such Event of Default and its status.

ARTICLE 14

SUBORDINATION OF SECURITIES

Section 14.01 Subordination Terms. The payment by the Company of the principal of, premium, if any, and interest on any series of Securities issued hereunder shall be subordinated to the extent set forth in an indenture supplemental hereto relating to such series.

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed all as of the day and year first above written.

AERPIO PHARMACEUTICALS, INC.

By: _____
Name: _____
Title: _____

AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC, as Trustee

By: _____
Name: _____
Title: _____

CROSS-REFERENCE TABLE (1)

Section of Trust Indenture Act of 1939, as Amended	Section of Indenture
310(a)	7.09
310(b)	7.08
	7.10
310(c)	Inapplicable
311(a)	7.13
311(b)	7.13
311(c)	Inapplicable
312(a)	5.01
	5.02(1)
312(b)	5.02(3)
312(c)	5.02(3)
313(a)	5.04(1)
313(b)	5.04(2)
313(c)	5.04(1)
	5.04(2)
313(d)	5.04(3)
314(a)	5.03
	13.12
314(b)	Inapplicable
314(c)	13.07(1)
314(d)	Inapplicable
314(e)	13.07(2)
314(f)	Inapplicable
315(a)	7.01(1)
	7.01(2)
315(b)	7.14
315(c)	7.01
315(d)	7.01(2)
315(e)	6.07
316(a)	6.06
	8.04
316(b)	6.04
316(c)	8.01
317(a)	6.02
317(b)	4.03
318(a)	13.09

(1) This Cross-Reference Table does not constitute part of the Indenture and shall not have any bearing on the interpretation of any of its terms or provisions.

Exhibit 4.6

AERPIO PHARMACEUTICALS, INC.
Issuer

AND

AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC,
Trustee

INDENTURE

Dated as of [●]

Senior Debt Securities

TABLE OF CONTENTS

(1) This Table of Contents does not constitute part of the Indenture and shall not have any bearing on the interpretation of any of its terms or provisions.

INDENTURE

INDENTURE, dated as of **[•]**, among **AERPIO PHARMACEUTICALS, INC.**, a Delaware corporation (the "**Company**"), and **AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC,** as trustee (the "**Trustee**"):

WHEREAS, for its lawful corporate purposes, the Company has duly authorized the execution and delivery of this Indenture to provide for the issuance of debt securities (hereinafter referred to as the "**Securities**"), in an unlimited aggregate principal amount to be issued from time to time in one or more series as in this Indenture provided, as registered Securities without coupons, to be authenticated by the certificate of the Trustee;

WHEREAS, to provide the terms and conditions upon which the Securities are to be authenticated, issued and delivered, the Company has duly authorized the execution of this Indenture; and

WHEREAS, all things necessary to make this Indenture a valid agreement of the Company, in accordance with its terms, have been done.

NOW, THEREFORE, in consideration of the premises and the purchase of the Securities by the holders thereof, it is mutually covenanted and agreed as follows for the equal and ratable benefit of the holders of Securities:

ARTICLE 1

DEFINITIONS

Section 1.01 Definitions of Terms.

The terms defined in this Section (except as in this Indenture or any indenture supplemental hereto otherwise expressly provided or unless the context otherwise requires) for all purposes of this Indenture and of any indenture supplemental hereto shall have the respective meanings specified in this Section and shall include the plural as well as the singular. All other terms used in this Indenture that are defined in the Trust Indenture Act of 1939, as amended, or that are by reference in such Act defined in the Securities Act of 1933, as amended (except as herein or any indenture supplemental hereto otherwise expressly provided or unless the context otherwise requires), shall have the meanings assigned to such terms in said Trust Indenture Act and in said Securities Act as in force at the date of the execution of this instrument.

"**Authenticating Agent**" means an authenticating agent with respect to all or any of the series of Securities appointed by the Trustee pursuant to Section 2.10.

"**Bankruptcy Law**" means Title 11, U.S. Code, or any similar federal or state law for the relief of debtors.

"**Board of Directors**" means the Board of Directors (or the functional equivalent thereof) of the Company or any duly authorized committee of such Board.

"**Board Resolution**" means a copy of a resolution certified by the Secretary or an Assistant Secretary of the Company to have been duly adopted by the Board of Directors and to be in full force and effect on the date of such certification.

"**Business Day**" means, with respect to any series of Securities, any day other than a day on which federal or state banking institutions in the Borough of Manhattan, the City of New York, or in the city of the Corporate Trust Office of the Trustee, are authorized or obligated by law, executive order or regulation to close.

"**Certificate**" means a certificate signed by any Officer. The Certificate need not comply with the provisions of Section 13.07.

"**Commission**" means the Securities and Exchange Commission, as from time to time constituted, created under the Exchange Act, or, if at any time after the execution of this instrument such Commission is not existing and performing the duties now assigned to it under the Trust Indenture Act, then the body performing such duties at such time.

"**Company**" means Aerpio Pharmaceuticals, Inc., a corporation duly organized and existing under the laws of the State of Delaware, and, subject to the provisions of Article Ten, shall also include its successors and assigns.

"**Corporate Trust Office**" means the office of the Trustee at which, at any particular time, its corporate trust business shall be principally administered, which office at the date hereof is located at 6201 15th Avenue, Brooklyn, New York 11219.

"**Custodian**" means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

"**Defaulted Interest**" has the meaning set forth in Section 2.03.

"**Depositary**" means, with respect to Securities of any series for which the Company shall determine that such Securities will be issued as a Global Security, The Depository Trust Company, another clearing agency, or any successor registered as a clearing agency under the Exchange Act, or other applicable statute or regulation, which, in each case, shall be designated by the Company pursuant to either Section 2.01 or 2.11.

"**Event of Default**" means, with respect to Securities of a particular series, any event specified in Section 6.01, continued for the period of time, if any, therein designated.

"**Exchange Act**" means the United States Securities and Exchange Act of 1934, as amended, and the rules and regulations promulgated by the Commission thereunder.

"**Global Security**" means a Security issued to evidence all or a part of any series of Securities which is executed by the Company and authenticated and delivered by the Trustee to the Depositary or pursuant to the Depositary's instruction, all in accordance with the Indenture, which shall be registered in the name of the Depositary or its nominee.

"**Governmental Obligations**" means securities that are (a) direct obligations of the United States of America for the payment of which its full faith and credit is pledged or (b) obligations of a Person controlled or supervised by and acting as an agency or instrumentality of the United States of America, the payment of which is unconditionally guaranteed as a full faith and credit obligation by the United States of America that, in either case, are not callable or redeemable at the option of the issuer thereof at any time prior to the stated maturity of the Securities, and shall also include a depositary receipt issued by a bank or trust company as custodian with respect to any such Governmental Obligation or a specific payment of principal of or interest on any such Governmental Obligation held by such custodian for the account of the holder of such depositary receipt; *provided*, *however*, that (except as required by law) such custodian is not authorized to make any deduction from the amount payable to the holder of such depositary receipt from any amount received by the custodian in respect of the Governmental Obligation or the specific payment of principal of or interest on the Governmental Obligation evidenced by such depositary receipt.

"**herein**", "**hereof**" and "**hereunder**", and other words of similar import, refer to this Indenture as a whole and not to any particular Article, Section or other subdivision.

"**Indenture**" means this instrument as originally executed or as it may from time to time be supplemented or amended by one or more indentures supplemental hereto entered into in accordance with the terms hereof and shall include the terms of particular series of Securities established as contemplated by Section 2.01.

"**Interest Payment Date**", when used with respect to any installment of interest on a Security of a particular series, means the date specified in such Security or in a Board Resolution or in an indenture supplemental hereto with respect to such series as the fixed date on which an installment of interest with respect to Securities of that series is due and payable.

"**Officer**" means, with respect to the Company, the chairman of the Board of Directors, a chief executive officer, a president, a chief financial officer, a chief operating officer, any executive vice president, any senior vice president, any vice president, the treasurer or any assistant treasurer, the controller or any assistant controller or the secretary or any assistant secretary.

"**Officer's Certificate**" means a certificate signed by any Officer. Each such certificate shall include the statements provided for in Section 13.07, if and to the extent required by the provisions thereof.

"**Opinion of Counsel**" means an opinion in writing subject to customary exceptions of legal counsel, who may be an employee of or counsel for the Company, that is delivered to the Trustee in accordance with the terms hereof. Each such opinion shall include the statements provided for in Section 13.07, if and to the extent required by the provisions thereof.

"**Outstanding**", when used with reference to Securities of any series, means, subject to the provisions of Section 8.04, as of any particular time, all Securities of that series theretofore authenticated and delivered by the Trustee under this Indenture, except (a) Securities theretofore canceled by the Trustee or any paying agent, or delivered to the Trustee or any paying agent for cancellation or that have previously been canceled; (b) Securities or portions thereof for the payment or redemption of which moneys or Governmental Obligations in the necessary amount shall have been deposited in trust with the Trustee or with any paying agent (other than the Company) or shall have been set aside and segregated in trust by the Company (if the Company shall act as its own paying agent); *provided*, *however*, that if such Securities or portions of such Securities are to be redeemed prior to the maturity thereof, notice of such redemption shall have been given as provided in Article Three, or provision satisfactory to the Trustee shall have been made for giving such notice; and (c) Securities in lieu of or in substitution for which other Securities shall have been authenticated and delivered pursuant to the terms of Section 2.07.

"**Person**" means any individual, corporation, partnership, joint venture, joint-stock company, limited liability company, association, trust, unincorporated organization, any other entity or organization, including a government or political subdivision or an agency or instrumentality thereof.

"**Predecessor Security**" of any particular Security means every previous Security evidencing all or a portion of the same debt as that evidenced by such particular Security; and, for the purposes of this definition, any Security authenticated and delivered under Section 2.07 in lieu of a lost, destroyed or stolen Security shall be deemed to evidence the same debt as the lost, destroyed or stolen Security.

"**Responsible Officer**" when used with respect to the Trustee means any officer of the Trustee assigned by the Trustee to administer its corporate trust matters with respect to this Indenture (which, for the avoidance of doubt, includes without limitation any supplemental indenture hereto).

"**Securities**" has the meaning stated in the first recital of this Indenture and more particularly means any Securities authenticated and delivered under this Indenture.

"**Securityholder**", "**holder of Securities**", "**registered holder**", or other similar term, means the Person or Persons in whose name or names a particular Security is registered on the Security Register kept for that purpose in accordance with the terms of this Indenture.

"**Security Register**" and "**Security Registrar**" shall have the meanings as set forth in Section 2.05.

"**Subsidiary**" means, with respect to any Person:

(1) any corporation or company a majority of whose capital stock with voting power, under ordinary circumstances, to elect directors is, at the date of determination, directly or indirectly, owned by such Person (a "**subsidiary**"), by one or more subsidiaries of such Person or by such Person and one or more subsidiaries of such Person;

(2) a partnership in which such Person or a subsidiary of such Person is, at the date of determination, a general partner of such partnership; or

(3) any partnership, limited liability company or other Person in which such Person, a subsidiary of such Person or such Person and one or more subsidiaries of such Person, directly or indirectly, at the date of determination, have (x) at least a majority ownership interest or (y) the power to elect or appoint or direct the election or appointment of the managing partner or member of such Person or, if applicable, a majority of the directors or other governing body of such Person.

"**Trustee**" means American Stock Transfer & Trust Company, LLC, and, subject to the provisions of Article Seven, shall also include its successors and assigns, and, if at any time there is more than one Person acting in such capacity hereunder, "Trustee" shall mean each such Person. The term "Trustee" as used with respect to a particular series of the Securities shall mean the trustee with respect to that series.

"**Trust Indenture Act**" means the Trust Indenture Act of 1939, as amended.

ARTICLE 2

ISSUE, DESCRIPTION, TERMS, EXECUTION, REGISTRATION AND EXCHANGE OF SECURITIES

Section 2.01 Designation and Terms of Securities.

(1) The aggregate principal amount of Securities that may be authenticated and delivered under this Indenture is unlimited. The Securities may be issued in one or more series up to the aggregate principal amount of Securities of that series from time to time authorized by or pursuant to a Board Resolution or pursuant to one or more indentures supplemental hereto. Prior to the initial issuance of Securities of any series, there shall be established in or pursuant to a Board Resolution, and set forth in an Officer's Certificate, or established in one or more indentures supplemental hereto:

(a) the title of the Securities of the series (which shall distinguish the Securities of that series from all other Securities);

(b) any limit upon the aggregate principal amount of the Securities of that series which may be authenticated and delivered under this Indenture (except for Securities authenticated and delivered upon registration of transfer of, or in exchange for, or in lieu of, other Securities of that series);

(c) the date or dates on which the principal of the Securities of the series is payable;

(d) if the price (expressed as a percentage of the aggregate principal amount thereof) at which such Securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such Securities that is convertible into another security or the method by which any such portion shall be determined;

(e) the rate or rates at which the Securities of the series shall bear interest or the manner of calculation of such rate or rates, if any;

(f) the date or dates from which such interest shall accrue, the Interest Payment Dates on which such interest will be payable or the manner of determination of such Interest Payment Dates, the place(s) of payment, and the record date for the determination of holders to whom interest is payable on any such Interest Payment Dates or the manner of determination of such record dates;

(g) the right, if any, to extend the interest payment periods and the duration of such extension;

(h) the period or periods within which, the price or prices at which and the terms and conditions upon which Securities of the series may be redeemed, converted or exchanged, in whole or in part;

(i) the obligation, if any, of the Company to redeem or purchase Securities of the series pursuant to any sinking fund, mandatory redemption, or analogous provisions (including payments made in cash in satisfaction of future sinking fund obligations) or at the option of a holder thereof and the period or periods within which, the price or prices at which, and the terms and conditions upon which, Securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

(j) the form of the Securities of the series including the form of the Certificate of Authentication for such series;

(k) if other than denominations of one thousand U.S. dollars ($1,000) or any integral multiple thereof, the denominations in which the Securities of the series shall be issuable;

(l) any and all other terms (including terms, to the extent applicable, relating to any auction or remarketing of the Securities of that series and any security for the obligations of the Company with respect to such Securities) with respect to such series (which terms shall not be inconsistent with the terms of this Indenture, as amended by any supplemental indenture) including any terms which may be required by or advisable under United States laws or regulations or advisable in connection with the marketing of Securities of that series;

(m) whether the Securities of the series shall be issued in whole or in part in the form of a Global Security or Securities; the terms and conditions, if any, upon which such Global Security or Securities may be exchanged in whole or in part for other individual Securities; and the Depositary for such Global Security or Securities;

(n) whether the Securities will be convertible into or exchangeable for shares of common stock, preferred stock or other securities of the Company or any other Person and, if so, the terms and conditions upon which such Securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at the Company's option or the holders' option) conversion or exchange features, and the applicable conversion or exchange period;

(o) if other than the full principal amount thereof, the portion of the principal amount of Securities of the series which shall be payable upon declaration of acceleration of the maturity thereof pursuant to Section 6.01;

(p) any additional or alternative events of default;

(q) additional or alternative covenants (which may include, among other restrictions, restrictions on the Company's ability or the ability of the Company's Subsidiaries to: incur additional indebtedness; issue additional securities; create liens; pay dividends or make distributions in respect of the capital stock of the Company or the Company's Subsidiaries; redeem capital stock; place restrictions on the Company's Subsidiaries' ability to pay dividends, make distributions or transfer assets; make investments or other restricted payments; sell or otherwise dispose of assets; enter into sale-leaseback transactions; engage in transactions with stockholders or affiliates; issue or sell stock of the Company's Subsidiaries; or effect a consolidation or merger) or financial covenants (which may include, among other financial covenants, financial covenants that require the Company and its Subsidiaries to maintain specified interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios) provided for with respect to the Securities of the series;

(r) the currency or currencies, including composite currencies, in which payment of the principal of (and premium, if any) and interest, if any, on such Securities shall be payable (if other than the currency of the United States of America), which unless otherwise specified shall be the currency of the United States of America as at the time of payment is legal tender for payment of public or private debts;

(s) if the principal of (and premium, if any) or interest, if any, on such Securities is to be payable, at the election of the Company or any Holder thereof, in a coin or currency other than that in which such Securities are stated to be payable, then the period or periods within which, and the terms and conditions upon which, such election may be made;

(t) whether interest will be payable in cash or additional Securities at the Company's or the Securityholders' option and the terms and conditions upon which the election may be made;

(u) the terms and conditions, if any, upon which the Company shall pay amounts in addition to the stated interest, premium, if any and principal amounts of the Securities of the series to any Securityholder that is not a "United States person" for federal tax purposes;

(v) additional or alternative provisions, if any, related to defeasance and discharge of the offered Securities;

(w) the applicability of any guarantees;

(x) any restrictions on transfer, sale or assignment of the Securities of the series; and

(y) any other terms of the series.

All Securities of any one series shall be substantially identical except as may otherwise be provided in or pursuant to any such Board Resolution or in any indentures supplemental hereto.

If any of the terms of the series are established by action taken pursuant to a Board Resolution of the Company, a copy of an appropriate record of such action shall be certified by the secretary or an assistant secretary of the Company and delivered to the Trustee at or prior to the delivery of the Officer's Certificate of the Company setting forth the terms of the series.

Securities of any particular series may be issued at various times, with different dates on which the principal or any installment of principal is payable, with different rates of interest, if any, or different methods by which rates of interest may be determined, with different dates on which such interest may be payable and with different redemption dates.

Section 2.02 Form of Securities and Trustee's Certificate.

The Securities of any series and the Trustee's certificate of authentication to be borne by such Securities shall be substantially of the tenor and purport as set forth in one or more indentures supplemental hereto or as provided in a Board Resolution, and set forth in an Officer's Certificate, and they may have such letters, numbers or other marks of identification or designation and such legends or endorsements printed, lithographed or engraved thereon as the Company may deem appropriate and as are not inconsistent with the provisions of this Indenture, or as may be required to comply with any law or with any rule or regulation made pursuant thereto or with any rule or regulation of any securities exchange on which Securities of that series may be listed, or to conform to usage.

Section 2.03 Denominations: Provisions for Payment.

The Securities shall be issuable as registered Securities and in the denominations of one thousand U.S. dollars ($1,000) or any integral multiple thereof, subject to Section 2.01(1)(j). The Securities of a particular series shall bear interest payable on the dates and at the rate specified with respect to that series. Subject to Section 2.01(1)(p), the principal of and the interest on the Securities of any series, as well as any premium thereon in case of redemption thereof prior to maturity, shall be payable in the coin or currency of the United States of America

that at the time is legal tender for public and private debt, at the office or agency of the Company maintained for that purpose. Each Security shall be dated the date of its authentication. Interest on the Securities shall be computed on the basis of a 360-day year composed of twelve 30-day months.

The interest installment on any Security that is payable, and is punctually paid or duly provided for, on any Interest Payment Date for Securities of that series shall be paid to the Person in whose name said Security (or one or more Predecessor Securities) is registered at the close of business on the regular record date for such interest installment. In the event that any Security of a particular series or portion thereof is called for redemption and the redemption date is subsequent to a regular record date with respect to any Interest Payment Date and prior to such Interest Payment Date, interest on such Security will be paid upon presentation and surrender of such Security as provided in Section 3.03.

Any interest on any Security that is payable, but is not punctually paid or duly provided for, on any Interest Payment Date for Securities of the same series (herein called "**Defaulted Interest**") shall forthwith cease to be payable to the registered holder on the relevant regular record date by virtue of having been such holder; and such Defaulted Interest shall be paid by the Company, at its election, as provided in clause (1) or clause (2) below:

(1) The Company may make payment of any Defaulted Interest on Securities to the Persons in whose names such Securities (or their respective Predecessor Securities) are registered at the close of business on a special record date for the payment of such Defaulted Interest, which shall be fixed in the following manner: the Company shall notify the Trustee in writing of the amount of Defaulted Interest proposed to be paid on each such Security and the date of the proposed payment, and at the same time the Company shall deposit with the Trustee an amount of money equal to the aggregate amount proposed to be paid in respect of such Defaulted Interest or shall make arrangements satisfactory to the Trustee for such deposit prior to the date of the proposed payment, such money when deposited to be held in trust for the benefit of the Persons entitled to such Defaulted Interest as in this clause provided. Thereupon the Trustee shall fix a special record date for the payment of such Defaulted Interest which shall not be more than 15 nor less than 10 days prior to the date of the proposed payment and not less than 10 days after the receipt by the Trustee of the notice of the proposed payment. The Trustee shall promptly notify the Company of such special record date and, in the name and at the expense of the Company, shall cause notice of the proposed payment of such Defaulted Interest and the special record date therefor to be mailed, first class postage prepaid, to each Securityholder at his or her address as it appears in the Security Register (as hereinafter defined), not less than 10 days prior to such special record date. Notice of the proposed payment of such Defaulted Interest and the special record date therefor having been mailed as aforesaid, such Defaulted Interest shall be paid to the Persons in whose names such Securities (or their respective Predecessor Securities) are registered on such special record date.

(2) The Company may make payment of any Defaulted Interest on any Securities in any other lawful manner not inconsistent with the requirements of any securities exchange on which such Securities may be listed, and upon such notice as may be required by such exchange, if, after notice given by the Company to the Trustee of the proposed payment pursuant to this clause, such manner of payment shall be deemed practicable by the Trustee.

Unless otherwise set forth in a Board Resolution or one or more indentures supplemental hereto establishing the terms of any series of Securities pursuant to Section 2.01 hereof, the term "**regular record date**" as used in this Section with respect to a series of Securities and any Interest Payment Date for such series shall mean either the fifteenth day of the month immediately preceding the month in which an Interest Payment Date established for such series pursuant to Section 2.01 hereof shall occur, if such Interest Payment Date is the first day of a month, or the first day of the month in which an Interest Payment Date established for such series pursuant to Section 2.01 hereof shall occur, if such Interest Payment Date is the fifteenth day of a month, whether or not such date is a Business Day.

Subject to the foregoing provisions of this Section, each Security of a series delivered under this Indenture upon transfer of or in exchange for or in lieu of any other Security of such series shall carry the rights to interest accrued and unpaid, and to accrue, that were carried by such other Security.

Section 2.04 Execution and Authentications.

The Securities shall be signed on behalf of the Company by one of its Officers. Signatures may be in the form of a manual or facsimile signature.

The Company may use the facsimile signature of any Person who shall have been an Officer, notwithstanding the fact that at the time the Securities shall be authenticated and delivered or disposed of such Person shall have ceased to be such an officer of the Company. The Securities may contain such notations, legends or endorsements required by law, stock exchange rule or usage. Each Security shall be dated the date of its authentication by the Trustee.

A Security shall not be valid until authenticated manually by an authorized signatory of the Trustee, or by an Authenticating Agent. Such signature shall be conclusive evidence that the Security so authenticated has been duly authenticated and delivered hereunder and that the holder is entitled to the benefits of this Indenture. At any time and from time to time after the execution and delivery of this Indenture, the Company may deliver Securities of any series executed by the Company to the Trustee for authentication, together with a written order of the Company for the authentication and delivery of such Securities, signed by an Officer, and the Trustee in accordance with such written order shall authenticate and deliver such Securities.

In authenticating such Securities and accepting the additional responsibilities under this Indenture in relation to such Securities, the Trustee shall be entitled to receive, if requested, and (subject to Section 7.01) shall be fully protected in relying upon, an Opinion of Counsel stating that the form and terms thereof have been established in conformity with the provisions of this Indenture.

The Trustee shall not be required to authenticate such Securities if the issue of such Securities pursuant to this Indenture will affect the Trustee's own rights, duties or immunities under the Securities and this Indenture or otherwise in a manner that is not reasonably acceptable to the Trustee.

Section 2.05 Registration of Transfer and Exchange.

(1) Securities of any series may be exchanged upon presentation thereof at the office or agency of the Company designated for such purpose, for other Securities of such series of authorized denominations, and for a like aggregate principal amount, upon payment of a sum sufficient to cover any tax or other governmental charge in relation thereto, all as provided in this Section. In respect of any Securities so surrendered for exchange, the Company shall execute, the Trustee shall authenticate and such office or agency shall deliver in exchange therefor the Security or Securities of the same series that the Securityholder making the exchange shall be entitled to receive, bearing numbers not contemporaneously outstanding.

(2) The Company shall keep, or cause to be kept, at its office or agency designated for such purpose a register or registers (herein referred to as the "**Security Register**") in which, subject to such reasonable regulations as it may prescribe, the Company shall register the Securities and the transfers of Securities as in this Article provided and which at all reasonable times shall be open for inspection by the Trustee. The registrar for the purpose of registering Securities and transfer of Securities as herein provided shall be appointed as authorized by Board Resolution (the "**Security Registrar**").

Upon surrender for transfer of any Security at the office or agency of the Company designated for such purpose, the Company shall execute, the Trustee shall authenticate and such office or agency shall deliver in the name of the transferee or transferees a new Security or Securities of the same series as the Security presented for a like aggregate principal amount.

All Securities presented or surrendered for exchange or registration of transfer, as provided in this Section, shall be accompanied (if so required by the Company or the Security Registrar) by a written instrument or instruments of transfer, in form satisfactory to the Company or the Security Registrar, duly executed by the registered holder or by such holder's duly authorized attorney in writing.

(3) Except as provided pursuant to Section 2.01 pursuant to a Board Resolution, and set forth in an Officer's Certificate, or established in one or more indentures supplemental to this Indenture, no service charge

shall be made for any exchange or registration of transfer of Securities, or issue of new Securities in case of partial redemption of any series, but the Company may require payment of a sum sufficient to cover any tax or other governmental charge in relation thereto, other than exchanges pursuant to Section 2.06, Section 3.03(2) and Section 9.04 not involving any transfer.

(4) The Company shall not be required (i) to issue, exchange or register the transfer of any Securities during a period beginning at the opening of business 15 days before the day of the mailing of a notice of redemption of less than all the Outstanding Securities of the same series and ending at the close of business on the day of such mailing, nor (ii) to register the transfer of or exchange any Securities of any series or portions thereof called for redemption, other than the unredeemed portion of any such Securities being redeemed in part. The provisions of this Section 2.05 are, with respect to any Global Security, subject to Section 2.11 hereof.

The Trustee shall have no obligation or duty to monitor, determine or inquire as to compliance with any restrictions on transfer imposed under this Indenture or under applicable law with respect to any transfer of any interest in any Security (including any transfers between or among depositary participants or beneficial owners of interests in any Global Security) other than to require delivery of such certificates and other documentation or evidence as are expressly required by, and to do so if and when expressly required by the terms of, this Indenture, and to examine the same to determine substantial compliance as to form with the express requirements hereof.

Section 2.06 Temporary Securities.

Pending the preparation of definitive Securities of any series, the Company may execute, and the Trustee shall authenticate and deliver, temporary Securities (printed, lithographed or typewritten) of any authorized denomination. Such temporary Securities shall be substantially in the form of the definitive Securities in lieu of which they are issued, but with such omissions, insertions and variations as may be appropriate for temporary Securities, all as may be determined by the Company. Every temporary Security of any series shall be executed by the Company and be authenticated by the Trustee upon the same conditions and in substantially the same manner, and with like effect, as the definitive Securities of such series. Without unnecessary delay the Company will execute and will furnish definitive Securities of such series and thereupon any or all temporary Securities of such series may be surrendered in exchange therefor (without charge to the holders), at the office or agency of the Company designated for the purpose, and the Trustee shall authenticate and such office or agency shall deliver in exchange for such temporary Securities an equal aggregate principal amount of definitive Securities of such series, unless the Company advises the Trustee to the effect that definitive Securities need not be executed and furnished until further notice from the Company. Until so exchanged, the temporary Securities of such series shall be entitled to the same benefits under this Indenture as definitive Securities of such series authenticated and delivered hereunder.

Section 2.07 Mutilated, Destroyed, Lost or Stolen Securities.

In case any temporary or definitive Security shall become mutilated or be destroyed, lost or stolen, the Company (subject to the next succeeding sentence) shall execute, and upon the Company's request the Trustee (subject as aforesaid) shall authenticate and deliver, a new Security of the same series, bearing a number not contemporaneously outstanding, in exchange and substitution for the mutilated Security, or in lieu of and in substitution for the Security so destroyed, lost or stolen. In every case the applicant for a substituted Security shall furnish to the Company and the Trustee such security or indemnity as may be required by them to save each of them harmless, and, in every case of destruction, loss or theft, the applicant shall also furnish to the Company and the Trustee evidence to their satisfaction of the destruction, loss or theft of the applicant's Security and of the ownership thereof. The Trustee may authenticate any such substituted Security and deliver the same upon the written request or authorization of any officer of the Company. Upon the issuance of any substituted Security, the Company may require the payment of a sum sufficient to cover any tax or other governmental charge that may be imposed in relation thereto and any other expenses (including the fees and expenses of the Trustee) connected therewith.

In case any Security that has matured or is about to mature shall become mutilated or be destroyed, lost or stolen, the Company may, instead of issuing a substitute Security, pay or authorize the payment of the same (without surrender thereof except in the case of a mutilated Security) if the applicant for such payment shall furnish to the Company and the Trustee such security or indemnity as they may require to save them harmless, and, in case of destruction, loss or theft, evidence to the satisfaction of the Company and the Trustee of the destruction, loss or theft of such Security and of the ownership thereof.

Every replacement Security issued pursuant to the provisions of this Section shall constitute an additional contractual obligation of the Company whether or not the mutilated, destroyed, lost or stolen Security shall be found at any time, or be enforceable by anyone, and shall be entitled to all the benefits of this Indenture equally and proportionately with any and all other Securities of the same series duly issued hereunder. All Securities shall be held and owned upon the express condition that the foregoing provisions are exclusive with respect to the replacement or payment of mutilated, destroyed, lost or stolen Securities, and shall preclude (to the extent lawful) any and all other rights or remedies, notwithstanding any law or statute existing or hereafter enacted to the contrary with respect to the replacement or payment of negotiable instruments or other securities without their surrender.

Section 2.08 Cancellation.

All Securities surrendered for the purpose of payment, redemption, exchange or registration of transfer shall, if surrendered to the Company or any paying agent, be delivered to the Trustee for cancellation, or, if surrendered to the Trustee, shall be cancelled by it, and no Securities shall be issued in lieu thereof except as expressly required or permitted by any of the provisions of this Indenture. On request of the Company at the time of such surrender, the Trustee shall deliver to the Company canceled Securities held by the Trustee. In the absence of such request the Trustee may dispose of canceled Securities in accordance with its standard procedures and deliver a certificate of disposition to the Company. If the Company shall otherwise acquire any of the Securities, however, such acquisition shall not operate as a redemption or satisfaction of the indebtedness represented by such Securities unless and until the same are delivered to the Trustee for cancellation.

Section 2.09 Benefits of Indenture.

Nothing in this Indenture or in the Securities, express or implied, shall give or be construed to give to any Person, other than the parties hereto and the holders of the Securities any legal or equitable right, remedy or claim under or in respect of this Indenture, or under any covenant, condition or provision herein contained; all such covenants, conditions and provisions being for the sole benefit of the parties hereto and of the holders of the Securities.

Section 2.10 Authenticating Agent.

So long as any of the Securities of any series remain Outstanding there may be an Authenticating Agent for any or all such series of Securities which the Trustee shall have the right to appoint. Said Authenticating Agent shall be authorized to act on behalf of the Trustee to authenticate Securities of such series issued upon exchange, transfer or partial redemption thereof, and Securities so authenticated shall be entitled to the benefits of this Indenture and shall be valid and obligatory for all purposes as if authenticated by the Trustee hereunder. All references in this Indenture to the authentication of Securities by the Trustee shall be deemed to include authentication by an Authenticating Agent for such series. Each Authenticating Agent shall be acceptable to the Company and shall be a corporation that has a combined capital and surplus, as most recently reported or determined by it, sufficient under the laws of any jurisdiction under which it is organized or in which it is doing business to conduct a trust business, and that is otherwise authorized under such laws to conduct such business and is subject to supervision or examination by federal or state authorities. If at any time any Authenticating Agent shall cease to be eligible in accordance with these provisions, it shall resign immediately.

Any Authenticating Agent may at any time resign by giving written notice of resignation to the Trustee and to the Company. The Trustee may at any time (and upon request by the Company shall) terminate the agency of any Authenticating Agent by giving written notice of termination to such Authenticating Agent and to the Company. Upon resignation, termination or cessation of eligibility of any Authenticating Agent, the Trustee may appoint an eligible successor Authenticating Agent acceptable to the Company. Any successor Authenticating Agent, upon acceptance of its appointment hereunder, shall become vested with all the rights, powers and duties of its predecessor hereunder as if originally named as an Authenticating Agent pursuant hereto.

Section 2.11 Global Securities.

(1) If the Company shall establish pursuant to Section 2.01 that the Securities of a particular series are to be issued as a Global Security, then the Company shall execute and the Trustee shall, in accordance with Section 2.04, authenticate and deliver, a Global Security that (i) shall represent, and shall be denominated in an amount equal to the aggregate principal amount of, all of the Outstanding Securities of such series, (ii) shall be registered in the name of the Depositary or its nominee, (iii) shall be delivered by the Trustee to the Depositary or pursuant to the Depositary's instruction and (iv) shall bear a legend substantially to the following effect: "Except as otherwise provided in Section 2.11 of the Indenture, this Security may be transferred, in whole but not in part, only to another nominee of the Depositary or to a successor Depositary or to a nominee of such successor Depositary."

(2) Notwithstanding the provisions of Section 2.05, the Global Security of a series may be transferred, in whole but not in part and in the manner provided in Section 2.05, only to another nominee of the Depositary for such series, or to a successor Depositary for such series selected or approved by the Company or to a nominee of such successor Depositary.

(3) If at any time the Depositary for a series of the Securities notifies the Company that it is unwilling or unable to continue as Depositary for such series or if at any time the Depositary for such series shall no longer be registered or in good standing under the Exchange Act, or other applicable statute or regulation, and a successor Depositary for such series is not appointed by the Company within 90 days after the Company receives such notice or becomes aware of such condition, as the case may be, or if an Event of Default has occurred and is continuing and the Company has received a request from the Depositary or from the Trustee, this Section 2.11 shall no longer be applicable to the Securities of such series and the Company will execute, and subject to Section 2.04, the Trustee will authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security. In addition, the Company may at any time determine that the Securities of any series shall no longer be represented by a Global Security and that the provisions of this Section 2.11 shall no longer apply to the Securities of such series. In such event the Company will execute and, subject to Section 2.04, the Trustee, upon receipt of an Officer's Certificate evidencing such determination by the Company, will authenticate and deliver the Securities of such series in definitive registered form without coupons, in authorized denominations, and in an aggregate principal amount equal to the principal amount of the Global Security of such series in exchange for such Global Security. Upon the exchange of the Global Security for such Securities in definitive registered form without coupons, in authorized denominations, the Global Security shall be canceled by the Trustee. Such Securities in definitive registered form issued in exchange for the Global Security pursuant to this Section 2.11(3) shall be registered in such names and in such authorized denominations as the Depositary, pursuant to instructions from its direct or indirect participants or otherwise, shall instruct the Trustee. The Trustee shall deliver such Securities to the Depositary for delivery to the Persons in whose names such Securities are so registered.

ARTICLE 3

REDEMPTION OF SECURITIES AND SINKING FUND PROVISIONS

Section 3.01 Redemption.

The Company may redeem the Securities of any series issued hereunder on and after the dates and in accordance with the terms established for such series pursuant to Section 2.01 hereof.

Section 3.02 Notice of Redemption.

(1) In case the Company shall desire to exercise such right to redeem all or, as the case may be, a portion of the Securities of any series in accordance with any right the Company reserved for itself to do so pursuant to Section 2.01 hereof, the Company shall, or shall cause the Trustee to, give notice of such redemption to holders of the Securities of such series to be redeemed by mailing, first class postage prepaid, a notice of such redemption not less than 30 days and not more than 90 days before the date fixed for redemption of that series to such holders at their last addresses as they shall appear upon the Security Register, unless a shorter period is specified in the Securities to be redeemed. Any notice that is mailed in the manner herein provided shall be

conclusively presumed to have been duly given, whether or not the registered holder receives the notice. In any case, failure duly to give such notice to the holder of any Security of any series designated for redemption in whole or in part, or any defect in the notice, shall not affect the validity of the proceedings for the redemption of any other Securities of such series or any other series. In the case of any redemption of Securities prior to the expiration of any restriction on such redemption provided in the terms of such Securities or elsewhere in this Indenture, the Company shall furnish the Trustee with an Officer's Certificate evidencing compliance with any such restriction.

Each such notice of redemption shall specify the date fixed for redemption and the redemption price at which Securities of that series are to be redeemed, and shall state that payment of the redemption price of such Securities to be redeemed will be made at the office or agency of the Company, upon presentation and surrender of such Securities, that interest accrued to the date fixed for redemption will be paid as specified in said notice, that from and after said date interest will cease to accrue and that the redemption is from a sinking fund, if such is the case. If less than all the Securities of a series are to be redeemed, the notice to the holders of Securities of that series to be redeemed in part shall specify the particular Securities to be so redeemed.

In case any Security is to be redeemed in part only, the notice that relates to such Security shall state the portion of the principal amount thereof to be redeemed, and shall state that on and after the redemption date, upon surrender of such Security, a new Security or Securities of such series in principal amount equal to the unredeemed portion thereof will be issued.

(2) If less than all the Securities of a series are to be redeemed, the Company shall give the Trustee at least 45 days' notice (unless a shorter notice shall be satisfactory to the Trustee) in advance of the date fixed for redemption as to the aggregate principal amount of Securities of the series to be redeemed, and thereupon the Trustee shall select, by lot or in such other manner as it shall deem appropriate and fair in its discretion and that may provide for the selection of a portion or portions (equal to one thousand U.S. dollars ($1,000) or any integral multiple thereof) of the principal amount of such Securities of a denomination larger than $1,000, the Securities to be redeemed and shall thereafter promptly notify the Company in writing of the numbers of the Securities to be redeemed, in whole or in part. The Company may, if and whenever it shall so elect, by delivery of instructions signed on its behalf by an Officer, instruct the Trustee or any paying agent to call all or any part of the Securities of a particular series for redemption and to give notice of redemption in the manner set forth in this Section, such notice to be in the name of the Company or its own name as the Trustee or such paying agent may deem advisable. In any case in which notice of redemption is to be given by the Trustee or any such paying agent, the Company shall deliver or cause to be delivered to, or permit to remain with, the Trustee or such paying agent, as the case may be, such Security Register, transfer books or other records, or suitable copies or extracts therefrom, sufficient to enable the Trustee or such paying agent to give any notice by mail that may be required under the provisions of this Section.

Section 3.03 Payment Upon Redemption.

(1) If the giving of notice of redemption shall have been completed as above provided, the Securities or portions of Securities of the series to be redeemed specified in such notice shall become due and payable on the date and at the place stated in such notice at the applicable redemption price, together with interest accrued to the date fixed for redemption and interest on such Securities or portions of Securities shall cease to accrue on and after the date fixed for redemption, unless the Company shall default in the payment of such redemption price and accrued interest with respect to any such Security or portion thereof. On presentation and surrender of such Securities on or after the date fixed for redemption at the place of payment specified in the notice, said Securities shall be paid and redeemed at the applicable redemption price for such series, together with interest accrued thereon to the date fixed for redemption (but if the date fixed for redemption is an interest payment date, the interest installment payable on such date shall be payable to the registered holder at the close of business on the applicable record date pursuant to Section 2.03).

(2) Upon presentation of any Security of such series that is to be redeemed in part only, the Company shall execute and the Trustee shall authenticate and the office or agency where the Security is presented shall deliver to the holder thereof, at the expense of the Company, a new Security of the same series of authorized denominations in principal amount equal to the unredeemed portion of the Security so presented.

Section 3.04 Sinking Fund.

The provisions of Sections 3.04, 3.05 and 3.06 shall be applicable to any sinking fund for the retirement of Securities of a series, except as otherwise specified as contemplated by Section 2.01 for Securities of such series.

The minimum amount of any sinking fund payment provided for by the terms of Securities of any series is herein referred to as a "**mandatory sinking fund payment**," and any payment in excess of such minimum amount provided for by the terms of Securities of any series is herein referred to as an "**optional sinking fund payment**". If provided for by the terms of Securities of any series, the cash amount of any sinking fund payment may be subject to reduction as provided in Section 3.05. Each sinking fund payment shall be applied to the redemption of Securities of any series as provided for by the terms of Securities of such series.

Section 3.05 Satisfaction of Sinking Fund Payments with Securities.

The Company (i) may deliver Outstanding Securities of a series and (ii) may apply as a credit Securities of a series that have been redeemed either at the election of the Company pursuant to the terms of such Securities or through the application of permitted optional sinking fund payments pursuant to the terms of such Securities, in each case in satisfaction of all or any part of any sinking fund payment with respect to the Securities of such series required to be made pursuant to the terms of such Securities as provided for by the terms of such series, provided that such Securities have not been previously so credited. Such Securities shall be received and credited for such purpose by the Trustee at the redemption price specified in such Securities for redemption through operation of the sinking fund and the amount of such sinking fund payment shall be reduced accordingly.

Section 3.06 Redemption of Securities for Sinking Fund.

Not less than 45 days prior to each sinking fund payment date for any series of Securities (unless a shorter period shall be satisfactory to the Trustee), the Company will deliver to the Trustee an Officer's Certificate specifying the amount of the next ensuing sinking fund payment for that series pursuant to the terms of the series, the portion thereof, if any, that is to be satisfied by delivering and crediting Securities of that series pursuant to Section 3.05 and the basis for such credit and will, together with such Officer's Certificate, deliver to the Trustee any Securities to be so delivered. Not less than 30 days before each such sinking fund payment date the Trustee shall select the Securities to be redeemed upon such sinking fund payment date in the manner specified in Section 3.02 and cause notice of the redemption thereof to be given in the name of and at the expense of the Company in the manner provided in Section 3.02. Such notice having been duly given, the redemption of such Securities shall be made upon the terms and in the manner stated in Section 3.03.

ARTICLE 4

COVENANTS

Section 4.01 Payment of Principal, Premium and Interest.

The Company will duly and punctually pay or cause to be paid the principal of (and premium, if any) and interest on the Securities of that series at the time and place and in the manner provided herein and established with respect to such Securities. Payments of principal on the Securities may be made at the time provided herein and established with respect to such Securities by U.S. dollar check drawn on and mailed to the address of the Securityholder entitled thereto as such address shall appear in the Security Register, or U.S. dollar wire transfer to, a U.S. dollar account if such Securityholder shall have furnished wire instructions to the Trustee no later than 15 days prior to the relevant payment date.

Payments of interest on the Securities may be made at the time provided herein and established with respect to such Securities by U.S. dollar check mailed to the address of the Securityholder entitled thereto as such address shall appear in the Security Register, or U.S. dollar wire transfer to, a U.S. dollar account if such Securityholder shall have furnished wire instructions in writing to the Security Registrar and the Trustee no later than 15 days prior to the relevant payment date.

Section 4.02 Maintenance of Office or Agency.

So long as any series of the Securities remain Outstanding, the Company agrees to maintain an office or agency with respect to each such series and at such other location or locations as may be designated as provided in this Section 4.02, where (i) Securities of that series may be presented for payment, (ii) Securities of that series may be presented as herein above authorized for registration of transfer and exchange, and (iii) notices and demands to or upon the Company in respect of the Securities of that series and this Indenture may be given or served, such designation to continue with respect to such office or agency until the Company shall, by written notice signed by any officer authorized to sign an Officer's Certificate and delivered to the Trustee, designate some other office or agency for such purposes or any of them. If at any time the Company shall fail to maintain any such required office or agency or shall fail to furnish the Trustee with the address thereof, such presentations, notices and demands may be made or served at the Corporate Trust Office of the Trustee, and the Company hereby appoints the Trustee as its agent to receive all such presentations, notices and demands. The Company initially appoints the Corporate Trust Office of the Trustee as its paying agent with respect to the Securities.

Section 4.03 Paying Agents.

(1) If the Company shall appoint one or more paying agents for all or any series of the Securities, other than the Trustee, the Company will cause each such paying agent to execute and deliver to the Trustee an instrument in which such agent shall agree with the Trustee, subject to the provisions of this Section:

(a) that it will hold all sums held by it as such agent for the payment of the principal of (and premium, if any) or interest on the Securities of that series (whether such sums have been paid to it by the Company or by any other obligor of such Securities) in trust for the benefit of the Persons entitled thereto;

(b) that it will give the Trustee notice of any failure by the Company (or by any other obligor of such Securities) to make any payment of the principal of (and premium, if any) or interest on the Securities of that series when the same shall be due and payable;

(c) that it will, at any time during the continuance of any failure referred to in the preceding paragraph (a)(2) above, upon the written request of the Trustee, forthwith pay to the Trustee all sums so held in trust by such paying agent; and

(d) that it will perform all other duties of paying agent as set forth in this Indenture.

(2) If the Company shall act as its own paying agent with respect to any series of the Securities, it will on or before each due date of the principal of (and premium, if any) or interest on Securities of that series, set aside, segregate and hold in trust for the benefit of the Persons entitled thereto a sum sufficient to pay such principal (and premium, if any) or interest so becoming due on Securities of that series until such sums shall be paid to such Persons or otherwise disposed of as herein provided and will promptly notify the Trustee of such action, or any failure (by it or any other obligor on such Securities) to take such action. Whenever the Company shall have one or more paying agents for any series of Securities, it will, prior to each due date of the principal of (and premium, if any) or interest on any Securities of that series, deposit with the paying agent a sum sufficient to pay the principal (and premium, if any) or interest so becoming due, such sum to be held in trust for the benefit of the Persons entitled to such principal, premium or interest, and (unless such paying agent is the Trustee) the Company will promptly notify the Trustee of this action or failure so to act.

(3) Notwithstanding anything in this Section to the contrary, (i) the agreement to hold sums in trust as provided in this Section is subject to the provisions of Section 11.05, and (ii) the Company may at any time, for the purpose of obtaining the satisfaction and discharge of this Indenture or for any other purpose, pay, or direct any paying agent to pay, to the Trustee all sums held in trust by the Company or such paying agent, such sums to be held by the Trustee upon the same terms and conditions as those upon which such sums were held by the Company or such paying agent; and, upon such payment by the Company or any paying agent to the Trustee, the Company or such paying agent shall be released from all further liability with respect to such money.

Section 4.04 Appointment to Fill Vacancy in Office of Trustee.

The Company, whenever necessary to avoid or fill a vacancy in the office of Trustee, will appoint, in the manner provided in Section 7.10, a Trustee, so that there shall at all times be a Trustee hereunder.

Section 4.05 Compliance with Consolidation Provisions.

The Company will not, while any of the Securities remain Outstanding, consolidate with or merge into any other Person, in either case where the Company is not the survivor of such transaction, or sell or convey all or substantially all of its property to any other Person unless the provisions of Article Ten hereof are complied with.

ARTICLE 5

SECURITYHOLDERS' LISTS AND REPORTS BY THE COMPANY AND THE TRUSTEE

Section 5.01 Company to Furnish Trustee Names and Addresses of Securityholders.

The Company will furnish or cause to be furnished to the Trustee (a) within 15 days after each regular record date (as defined in Section 2.03) a list, in such form as the Trustee may reasonably require, of the names and addresses of the holders of each series of Securities as of such regular record date, *provided* that the Company shall not be obligated to furnish or cause to furnish such list at any time that the list shall not differ in any respect from the most recent list furnished to the Trustee by the Company and (b) at such other times as the Trustee may request in writing within 30 days after the receipt by the Company of any such request, a list of similar form and content as of a date not more than 15 days prior to the time such list is furnished; *provided*, *however*, that, in either case, no such list need be furnished for any series for which the Trustee shall be the Security Registrar.

Section 5.02 Preservation Of Information; Communications With Securityholders.

(1) The Trustee shall preserve, in as current a form as is reasonably practicable, all information as to the names and addresses of the holders of Securities contained in the most recent list furnished to it as provided in Section 5.01 and as to the names and addresses of holders of Securities received by the Trustee in its capacity as Security Registrar (if acting in such capacity).

(2) The Trustee may destroy any list furnished to it as provided in Section 5.01 upon receipt of a new list so furnished.

(3) Securityholders may communicate as provided in Section 312(b) of the Trust Indenture Act with other Securityholders with respect to their rights under this Indenture or under the Securities, and, in connection with any such communications, the Trustee shall satisfy its obligations under Section 312(b) of the Trust Indenture Act in accordance with the provisions of Section 312(b) of the Trust Indenture Act.

Section 5.03 Reports by the Company.

(1) The Company covenants and agrees to provide (which delivery may be via electronic mail) to the Trustee within 30 days, after the Company files the same with the Commission, copies of the annual reports and of the information, documents and other reports (or copies of such portions of any of the foregoing as the Commission may from time to time by rules and regulations prescribe) that the Company is required to file with the Commission pursuant to Section 13 or Section 15(d) of the Exchange Act; *provided*, *however*, the Company shall not be required to deliver to the Trustee any materials for which the Company has sought and received confidential treatment by the Commission; and *provided further*, that so long as such filings by the Company are available on the Commission's Electronic Data Gathering, Analysis and Retrieval System (EDGAR), or Interactive Data Electronic Applications (IDEA), or any successor system, such filings shall be deemed to have been filed with the Trustee for purposes hereof without any further action required by the Company; *provided* that an electronic link to such filing, together with an electronic notice of such filing have been sent to the Trustee. For the avoidance of doubt, a failure by the Company to file annual reports, information and other reports with the SEC within the time period prescribed thereof by the Commission shall not be deemed a breach of this Section 5.03.

(2) Delivery of reports, information and documents to the Trustee under Section 5.03 is for informational purposes only and the information and the Trustee's receipt of the foregoing shall not constitute constructive notice of any information contained therein, or determinable from information contained therein including the Company's compliance with any of their covenants thereunder (as to which the Trustee is entitled to rely exclusively on an Officer's Certificate).

Section 5.04 Reports by the Trustee.

(1) If required by Section 313(a) of the Trust Indenture Act, the Trustee, within sixty (60) days after each May 1, shall transmit by mail, first class postage prepaid, to the Securityholders, as their names and addresses appear upon the Security Register, a brief report dated as of such May 1, which complies with Section 313(a) of the Trust Indenture Act.

(2) The Trustee shall comply with Section 313(b) and 313(c) of the Trust Indenture Act.

(3) A copy of each such report shall, at the time of such transmission to Securityholders, be filed by the Trustee with the Company, with each securities exchange upon which any Securities are listed (if so listed) and also with the Commission. The Company agrees to notify the Trustee when any Securities become listed on any securities exchange.

ARTICLE 6

REMEDIES OF THE TRUSTEE AND SECURITYHOLDERS ON EVENT OF DEFAULT

Section 6.01 Events of Default.

(1) Whenever used herein with respect to Securities of a particular series, "**Event of Default**" means any one or more of the following events that has occurred and is continuing:

(a) the Company defaults in the payment of any installment of interest upon any of the Securities of that series, as and when the same shall become due and payable, and such default continues for a period of 90 days; *provided*, *however*, that a valid extension of an interest payment period by the Company in accordance with the terms of any indenture supplemental hereto shall not constitute a default in the payment of interest for this purpose;

(b) the Company defaults in the payment of the principal of (or premium, if any, on) any of the Securities of that series as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to that series; *provided*, *however*, that a valid extension of the maturity of such Securities in accordance with the terms of any indenture supplemental hereto shall not constitute a default in the payment of principal or premium, if any;

(c) the Company fails to observe or perform any other of its covenants or agreements with respect to that series contained in this Indenture or otherwise established with respect to that series of Securities pursuant to Section 2.01 hereof (other than a covenant or agreement that has been expressly included in this Indenture solely for the benefit of one or more series of Securities other than such series) for a period of 90 days after the date on which written notice of such failure, requiring the same to be remedied and stating that such notice is a "**Notice of Default**" hereunder, shall have been given to the Company by the Trustee, by registered or certified mail, or to the Company and the Trustee by the holders of at least 25% in principal amount of the Securities of that series at the time Outstanding;

(d) the Company pursuant to or within the meaning of any Bankruptcy Law (i) commences a voluntary case, (ii) consents to the entry of an order for relief against it in an involuntary case, (iii) consents to the appointment of a Custodian of it or for all or substantially all of its property or (iv) makes a general assignment for the benefit of its creditors; or

(e) a court of competent jurisdiction enters an order under any Bankruptcy Law that (i) is for relief against the Company in an involuntary case, (ii) appoints a Custodian of the Company for all or substantially all of its property or (iii) orders the liquidation of the Company, and the order or decree remains unstayed and in effect for 90 days.

(2) In each and every such case (other than an Event of Default specified in clause (4) or clause (5) above), unless the principal of all the Securities of that series shall have already become due and payable, either the Trustee or the holders of not less than 25% in aggregate principal amount of the Securities of that series then Outstanding hereunder, by notice in writing to the Company (and to the Trustee if given by such Securityholders), may declare the principal of (and premium, if any, on) and accrued and unpaid interest on all the Securities of that series to be due and payable immediately, and upon any such declaration the same shall become and shall be immediately due and payable. If an Event of Default specified in clause (4) or clause (5) above occurs, the principal of and accrued and unpaid interest on all the Securities of that series shall automatically be immediately due and payable without any declaration or other act on the part of the Trustee or the holders of the Securities.

(3) At any time after the principal of (and premium, if any, on) and accrued and unpaid interest on the Securities of that series shall have been so declared due and payable, and before any judgment or decree for the payment of the moneys due shall have been obtained or entered as hereinafter provided, the holders of a majority in aggregate principal amount of the Securities of that series then Outstanding hereunder, by written notice to the Company and the Trustee, may rescind and annul such declaration and its consequences if: (i) the Company has paid or deposited with the Trustee a sum sufficient to pay all matured installments of interest upon all the Securities of that series and the principal of (and premium, if any, on) any and all Securities of that series that shall have become due otherwise than by acceleration (with interest upon such principal and premium, if any, and, to the extent that such payment is enforceable under applicable law, upon overdue installments of interest, at the rate per annum expressed in the Securities of that series to the date of such payment or deposit) and the amount payable to the Trustee under Section 7.06, and (ii) any and all Events of Default under the Indenture with respect to such series, other than the nonpayment of principal on (and premium, if any, on) and accrued and unpaid interest on Securities of that series that shall not have become due by their terms, shall have been remedied or waived as provided in Section 6.06.

No such rescission and annulment shall extend to or shall affect any subsequent default or impair any right consequent thereon.

(4) In case the Trustee shall have proceeded to enforce any right with respect to Securities of that series under this Indenture and such proceedings shall have been discontinued or abandoned because of such rescission or annulment or for any other reason or shall have been determined adversely to the Trustee, then and in every such case, subject to any determination in such proceedings, the Company and the Trustee shall be restored respectively to their former positions and rights hereunder, and all rights, remedies and powers of the Company and the Trustee shall continue as though no such proceedings had been taken.

Section 6.02 Collection of Indebtedness and Suits for Enforcement by Trustee.

(1) The Company covenants that (i) in case it shall default in the payment of any installment of interest on any of the Securities of a series, or in any payment required by any sinking or analogous fund established with respect to that series as and when the same shall have become due and payable, and such default shall have continued for a period of 90 days, or (ii) in case it shall default in the payment of the principal of (or premium, if any, on) any of the Securities of a series when the same shall have become due and payable, whether upon maturity of the Securities of a series or upon redemption or upon declaration or otherwise then, upon demand of the Trustee, the Company will pay to the Trustee, for the benefit of the holders of the Securities of that series, the whole amount that then shall have been become due and payable on all such Securities for principal (and premium, if any) or interest, or both, as the case may be, with interest upon the overdue principal (and premium, if any) and (to the extent that payment of such interest is enforceable under applicable law) upon overdue installments of interest at the rate per annum expressed in the Securities of that series; and, in addition thereto, such further amount as shall be sufficient to cover the costs and expenses of collection, and the amount payable to the Trustee under Section 7.06.

(2) If the Company shall fail to pay such amounts forthwith upon such demand, the Trustee, in its own name and as trustee of an express trust, shall be entitled and empowered to institute any action or proceedings at law or in equity for the collection of the sums so due and unpaid, and may prosecute any such action or proceeding to judgment or final decree, and may enforce any such judgment or final decree against the Company or other obligor upon the Securities of that series and collect the moneys adjudged or decreed to be payable in the manner provided by law or equity out of the property of the Company or other obligor upon the Securities of that series, wherever situated.

(3) In case of any receivership, insolvency, liquidation, bankruptcy, reorganization, readjustment, arrangement, composition or judicial proceedings affecting the Company, or its creditors or property, the Trustee shall have power to intervene in such proceedings and take any action therein that may be permitted by the court and shall (except as may be otherwise provided by law) be entitled to file such proofs of claim and other papers and documents as may be necessary or advisable in order to have the claims of the Trustee and of the holders of Securities of such series allowed for the entire amount due and payable by the Company under the Indenture at the date of institution of such proceedings and for any additional amount that may become due and payable by the Company after such date, and to collect and receive any moneys or other property payable or deliverable on any such claim, and to distribute the same after the deduction of the amount payable to the Trustee under Section 7.06; and any receiver, assignee or trustee in bankruptcy or reorganization is hereby authorized by each of the holders of Securities of such series to make such payments to the Trustee, and, in the event that the Trustee shall consent to the making of such payments directly to such Securityholders, to pay to the Trustee any amount due it under Section 7.06.

(4) All rights of action and of asserting claims under this Indenture, or under any of the terms established with respect to Securities of that series, may be enforced by the Trustee without the possession of any of such Securities, or the production thereof at any trial or other proceeding relative thereto, and any such suit or proceeding instituted by the Trustee shall be brought in its own name as trustee of an express trust, and any recovery of judgment shall, after provision for payment to the Trustee of any amounts due under Section 7.06, be for the ratable benefit of the holders of the Securities of such series.

In case of an Event of Default hereunder, the Trustee may in its discretion proceed to protect and enforce the rights vested in it by this Indenture by such appropriate judicial proceedings as the Trustee shall deem most effectual to protect and enforce any of such rights, either at law or in equity or in bankruptcy or otherwise, whether for the specific enforcement of any covenant or agreement contained in the Indenture or in aid of the exercise of any power granted in this Indenture, or to enforce any other legal or equitable right vested in the Trustee by this Indenture or by law.

Nothing contained herein shall be deemed to authorize the Trustee to authorize or consent to or accept or adopt on behalf of any Securityholder any plan of reorganization, arrangement, adjustment or composition affecting the Securities of that series or the rights of any holder thereof or to authorize the Trustee to vote in respect of the claim of any Securityholder in any such proceeding.

Section 6.03 Application of Moneys Collected.

Any moneys collected by the Trustee pursuant to this Article with respect to a particular series of Securities shall be applied in the following order, at the date or dates fixed by the Trustee and, in case of the distribution of such moneys on account of principal (or premium, if any) or interest, upon presentation of the Securities of that series, and notation thereon of the payment, if only partially paid, and upon surrender thereof if fully paid:

FIRST: To the payment of reasonable costs and expenses of collection and of all amounts payable to the Trustee under Section 7.06;

SECOND: To the payment of the amounts then due and unpaid upon Securities of such series for principal (and premium, if any) and interest, in respect of which or for the benefit of which such money has been collected, ratably, without preference or priority of any kind, according to the amounts due and payable on such Securities for principal (and premium, if any) and interest, respectively; and

THIRD: To the payment of the remainder, if any, to the Company or any other Person lawfully entitled thereto.

Section 6.04 Limitation on Suits.

No holder of any Security of any series shall have any right by virtue or by availing of any provision of this Indenture or any Security to institute any suit, action or proceeding in equity or at law upon or under or with respect to this Indenture, any Security or for the appointment of a receiver or trustee, or for any other remedy hereunder, unless (i) such holder previously shall have given to the Trustee written notice of an Event of Default and of the continuance thereof with respect to the Securities of such series specifying such Event of Default, as hereinbefore provided; (ii) the holders of not less than 25% in aggregate principal amount of the Securities of such series then Outstanding shall have made written request upon the Trustee to institute such action, suit or proceeding in its own name as Trustee hereunder; (iii) such holder or holders shall have offered to the Trustee such reasonable indemnity as it may require against the costs, expenses and liabilities to be incurred therein or thereby; (iv) the Trustee for 90 days after its receipt of such notice, request and offer of indemnity, shall have failed to institute any such action, suit or proceeding and (v) during such 90 day period, the holders of a majority in principal amount of the Securities of that series do not give the Trustee a direction inconsistent with the request.

Notwithstanding anything contained herein to the contrary or any other provisions of this Indenture, the right of any holder of any Security to receive payment of the principal of (and premium, if any) and interest on such Security, as therein provided, on or after the respective due dates expressed in such Security (or in the case of redemption, on the redemption date), or to institute suit for the enforcement of any such payment on or after such respective dates or redemption date, shall not be impaired or affected without the consent of such holder and by accepting a Security hereunder it is expressly understood, intended and covenanted by the taker and holder of every Security of such series with every other such taker and holder and the Trustee, that no one or more holders of Securities of such series shall have any right in any manner whatsoever by virtue or by availing of any provision of this Indenture to affect, disturb or prejudice the rights of the holders of any other of such Securities, or to obtain or seek to obtain priority over or preference to any other such holder, or to enforce any right under this Indenture, except in the manner herein provided and for the equal, ratable and common benefit of all holders of Securities of such series. For the protection and enforcement of the provisions of this Section, each and every Securityholder and the Trustee shall be entitled to such relief as can be given either at law or in equity.

Section 6.05 Rights and Remedies Cumulative; Delay or Omission Not Waiver.

(1) Except as otherwise provided in Section 2.07, all powers and remedies given by this Article to the Trustee or to the Securityholders shall, to the extent permitted by law, be deemed cumulative and not exclusive of any other powers and remedies available to the Trustee or the holders of the Securities, by judicial proceedings or otherwise, to enforce the performance or observance of the covenants and agreements contained in this Indenture or otherwise established with respect to such Securities.

(2) No delay or omission of the Trustee or of any holder of any of the Securities to exercise any right or power accruing upon any Event of Default occurring and continuing as aforesaid shall impair any such right or power, or shall be construed to be a waiver of any such default or an acquiescence therein; and, subject to the provisions of Section 6.04, every power and remedy given by this Article or by law to the Trustee or the Securityholders may be exercised from time to time, and as often as shall be deemed expedient, by the Trustee or by the Securityholders.

Section 6.06 Control by Securityholders.

The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding, determined in accordance with Section 8.04, shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred on the Trustee with respect to such series; *provided*, *however*, that such direction shall not be in conflict with any rule of law or with this Indenture or subject the Trustee in its sole discretion to personal liability. Subject to the provisions of Section 7.01, the Trustee shall have the right to decline to follow any such direction if the Trustee in

good faith shall, by a Responsible Officer or officers of the Trustee, determine that the proceeding so directed, subject to the Trustee's duties under the Trust Indenture Act, would involve the Trustee in personal liability or might be unduly prejudicial to the Securityholders not involved in the proceeding. The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding affected thereby, determined in accordance with Section 8.04, may on behalf of the holders of all of the Securities of such series waive any past default in the performance of any of the covenants contained herein or established pursuant to Section 2.01 with respect to such series and its consequences, except a default in the payment of the principal of, or premium, if any, or interest on, any of the Securities of that series as and when the same shall become due by the terms of such Securities otherwise than by acceleration (unless such default has been cured and a sum sufficient to pay all matured installments of interest and principal and any premium has been deposited with the Trustee (in accordance with Section 6.01(3)). Upon any such waiver, the default covered thereby shall be deemed to be cured for all purposes of this Indenture and the Company, the Trustee and the holders of the Securities of such series shall be restored to their former positions and rights hereunder, respectively; but no such waiver shall extend to any subsequent or other default or impair any right consequent thereon.

Section 6.07 Undertaking to Pay Costs.

All parties to this Indenture agree, and each holder of any Securities by such holder's acceptance thereof shall be deemed to have agreed, that any court may in its discretion require, in any suit for the enforcement of any right or remedy under this Indenture, or in any suit against the Trustee for any action taken or omitted by it as Trustee, the filing by any party litigant in such suit of an undertaking to pay the costs of such suit, and that such court may in its discretion assess reasonable costs, including reasonable attorneys' fees, against any party litigant in such suit, having due regard to the merits and good faith of the claims or defenses made by such party litigant; but the provisions of this Section shall not apply to any suit instituted by the Trustee, to any suit instituted by any Securityholder, or group of Securityholders, holding more than 10% in aggregate principal amount of the Outstanding Securities of any series, or to any suit instituted by any Securityholder for the enforcement of the payment of the principal of (or premium, if any) or interest on any Security of such series, on or after the respective due dates expressed in such Security or established pursuant to this Indenture.

ARTICLE 7

CONCERNING THE TRUSTEE

Section 7.01 Certain Duties and Responsibilities of Trustee.

(1) The Trustee, prior to the occurrence of an Event of Default with respect to the Securities of a series and after the curing of all Events of Default with respect to the Securities of that series that may have occurred, shall undertake to perform with respect to the Securities of such series such duties and only such duties as are specifically set forth in this Indenture, and no implied covenants shall be read into this Indenture against the Trustee. In case an Event of Default with respect to the Securities of a series has occurred (that has not been cured or waived), the Trustee shall exercise with respect to Securities of that series such of the rights and powers vested in it by this Indenture, and use the same degree of care and skill in their exercise, as a prudent man would exercise or use under the circumstances in the conduct of his own affairs.

(2) No provision of this Indenture shall be construed to relieve the Trustee from liability for its own gross negligence, or its own willful misconduct, except that:

(a) prior to the occurrence of an Event of Default with respect to the Securities of a series and after the curing or waiving of all such Events of Default with respect to that series that may have occurred:

(A) the duties and obligations of the Trustee shall with respect to the Securities of such series be determined solely by the express provisions of this Indenture, and the Trustee shall not be liable with respect to the Securities of such series except for the performance of such duties and obligations as are specifically set forth in this Indenture, and no implied covenants or obligations shall be read into this Indenture against the Trustee; and

(B) in the absence of bad faith on the part of the Trustee, the Trustee may with respect to the Securities of such series conclusively rely, as to the truth of the statements and the correctness of the opinions expressed therein, upon any certificates or opinions furnished to the Trustee and conforming to the requirements of this Indenture; but in the case of any such certificates or opinions that by any provision hereof are specifically required to be furnished to the Trustee, the Trustee shall be under a duty to examine the same to determine in good faith whether or not, in the Trustee's reasonable judgment, they conform to the requirements of this Indenture;

(b) the Trustee shall not be liable for any error of judgment made in good faith by a Responsible Officer or Responsible Officers of the Trustee, unless it shall be proved that the Trustee was grossly negligent in ascertaining the pertinent facts;

(c) the Trustee shall not be liable with respect to any action taken or omitted to be taken by it in good faith in accordance with the direction of the holders of not less than a majority in principal amount of the Securities of any series at the time Outstanding relating to the time, method and place of conducting any proceeding for any remedy available to the Trustee, or exercising any trust or power conferred upon the Trustee under this Indenture with respect to the Securities of that series; and

(d) none of the provisions contained in this Indenture shall require the Trustee to expend or risk its own funds or otherwise incur personal financial liability in the performance of any of its duties or in the exercise of any of its rights or powers if there is reasonable ground for believing that the repayment of such funds or liability is not reasonably assured to it under the terms of this Indenture or adequate indemnity against such risk is not reasonably assured to it.

Section 7.02 Certain Rights of Trustee.

Except as otherwise provided in Section 7.01:

(1) The Trustee may rely and shall be fully protected and indemnified in acting or refraining from acting upon any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, approval, bond, security or other paper or document believed by it to be genuine and to have been signed or presented by the proper party or parties;

(2) Any request, direction, order or demand of the Company mentioned herein shall be sufficiently evidenced by a Board Resolution or an instrument signed in the name of the Company by any authorized officer of the Company (unless other evidence in respect thereof is specifically prescribed herein);

(3) The Trustee may consult with counsel and the written advice of such counsel or, if requested, any Opinion of Counsel shall be full and complete authorization and protection in respect of any action taken or suffered or omitted hereunder in good faith and in reliance thereon;

(4) The Trustee shall be under no obligation to exercise any of the rights or powers vested in it by this Indenture at the request, order or direction of any of the Securityholders pursuant to the provisions of this Indenture, unless such Securityholders shall have offered to the Trustee reasonable security or indemnity against the costs, expenses and liabilities that may be incurred therein or thereby; nothing contained herein shall, however, relieve the Trustee of the obligation, upon the occurrence of an Event of Default with respect to a series of the Securities (that has not been cured or waived), to exercise with respect to Securities of that series such of the rights and powers vested in it by this Indenture, and to use the same degree of care and skill in their exercise, as a prudent man would exercise or use under the circumstances in the conduct of his own affairs;

(5) The Trustee shall not be liable for any action taken or omitted to be taken by it in good faith and believed by it to be authorized or within the discretion or rights or powers conferred upon it by this Indenture;

(6) The Trustee shall not be bound to make any investigation into the facts or matters stated in any resolution, certificate, statement, instrument, opinion, report, notice, request, consent, order, approval, bond, security, or other papers or documents, unless requested in writing so to do by the holders of not less than a majority in principal amount of the Outstanding Securities of the particular series affected thereby (determined as provided in Section 8.04); *provided*, *however*, that if the payment within a reasonable time to the Trustee of the costs, expenses or liabilities likely to be incurred by it in the making of such investigation is, in the opinion of the Trustee, not reasonably assured to the Trustee by the security afforded to it by the terms of this Indenture, the Trustee may require reasonable indemnity against such costs, expenses or liabilities as a condition to so proceeding. The reasonable expense of every such examination shall be paid by the Company or, if paid by the Trustee, shall be repaid by the Company upon demand;

(7) The Trustee may execute any of the trusts or powers hereunder or perform any duties hereunder either directly or by or through agents or attorneys and the Trustee shall not be responsible for any misconduct or negligence on the part of any agent or attorney appointed with due care by it hereunder;

(8) In no event shall the Trustee be responsible or liable for any failure or delay in the performance of its obligations hereunder arising out of or caused by, directly or indirectly, forces beyond its control, including, without limitation, strikes, work stoppages, accidents, acts of war or terrorism, civil or military disturbances, nuclear or natural catastrophes or acts of God, and interruptions, loss or malfunctions of utilities, communications or computer (software and hardware) services; it being understood that the Trustee shall use reasonable efforts which are consistent with accepted practices in the banking industry to resume performance as soon as practicable under the circumstances;

(9) In no event shall the Trustee be responsible or liable for special, indirect, or consequential loss or damage of any kind whatsoever (including, but not limited to, loss of profit) irrespective of whether the Trustee has been advised of the likelihood of such loss or damage and regardless of the form of action; and

(10) The Trustee agrees to accept and act upon instructions or directions pursuant to this Indenture sent by unsecured e-mail, facsimile transmission or other similar unsecured electronic methods; *provided*, *however*, that (a) the party providing such written instructions, subsequent to such transmission of written instructions, shall provide the originally executed instructions or directions to the Trustee in a timely manner, and (b) such originally executed instructions or directions shall be signed by an authorized representative of the party providing such instructions or directions. If the party elects to give the Trustee e-mail or facsimile instructions (or instructions by a similar electronic method) and the Trustee in its discretion elects to act upon such instructions, the Trustee's understanding of such instructions shall be deemed controlling. The Trustee shall not be liable for any losses, costs or expenses arising directly or indirectly from the Trustee's reliance upon and compliance with such instructions notwithstanding such instructions conflict or are inconsistent with a subsequent written instruction. The party providing electronic instructions agrees to assume all risks arising out of the use of such electronic methods to submit instructions and directions to the Trustee, including without limitation the risk of the Trustee acting on unauthorized instructions, and the risk or interception and misuse by third parties.

In addition, the Trustee shall not be deemed to have knowledge of any Default or Event of Default until the Trustee shall have received written notification in the manner set forth in this Indenture or a Responsible Officer of the Trustee shall have obtained actual knowledge.

Section 7.03 Trustee Not Responsible for Recitals or Issuance or Securities.

(1) The recitals contained herein and in the Securities shall be taken as the statements of the Company, and the Trustee assumes no responsibility for the correctness of the same.

(2) The Trustee makes no representations as to the validity or sufficiency of this Indenture or of the Securities.

The Trustee shall not be accountable for the use or application by the Company of any of the Securities or of the proceeds of such Securities, or for the use or application of any moneys paid over by the Trustee in accordance with any provision of this Indenture or established pursuant to Section 2.01, or for the use or application of any moneys received by any paying agent other than the Trustee.

Section 7.04 May Hold Securities.

The Trustee or any paying agent or Security Registrar, in its individual or any other capacity, may become the owner or pledgee of Securities with the same rights it would have if it were not Trustee, paying agent or Security Registrar.

Section 7.05 Moneys Held in Trust.

Subject to the provisions of Section 11.05, all moneys received by the Trustee shall, until used or applied as herein provided, be held in trust for the purposes for which they were received, but need not be segregated from other funds except to the extent required by law. The Trustee shall be under no liability for interest on any moneys received by it hereunder except such as it may agree with the Company to pay thereon.

Section 7.06 Compensation and Reimbursement.

(1) The Company covenants and agrees to pay to the Trustee, and the Trustee shall be entitled to, such reasonable compensation (which shall not be limited by any provision of law in regard to the compensation of a trustee of an express trust) as the Company and the Trustee may from time to time agree in writing, for all services rendered by it in the execution of the trusts hereby created and in the exercise and performance of any of the powers and duties hereunder of the Trustee, and, except as otherwise expressly provided herein, the Company will pay or reimburse the Trustee upon its request for all reasonable expenses, disbursements and advances incurred or made by the Trustee in accordance with any of the provisions of this Indenture (including the reasonable compensation and the expenses and disbursements of its counsel and of all Persons not regularly in its employ), except any such expense, disbursement or advance as may arise from its negligence or bad faith and except as the Company and Trustee may from time to time agree in writing. The Company also covenants to indemnify the Trustee (and its officers, agents, directors and employees) for, and to hold it harmless against, any loss, liability or expense incurred without gross negligence or bad faith on the part of the Trustee and arising out of or in connection with the acceptance or administration of this trust, including the reasonable costs and expenses of defending itself against any claim of liability in the premises.

(2) The obligations of the Company under this Section to compensate and indemnify the Trustee and to pay or reimburse the Trustee for reasonable expenses, disbursements and advances shall constitute additional indebtedness hereunder. Such additional indebtedness shall be secured by a lien prior to that of the Securities upon all property and funds held or collected by the Trustee as such, except funds held in trust for the benefit of the holders of particular Securities.

(3) To ensure the Company's payment obligations in this Section, the Trustee shall have a lien prior to the Securities on all funds or property held or collected by the Trustee, except that held in trust to pay principal of or interest on particular Securities. When the Trustee incurs expenses or renders services in connection with an Event of Default specified in Section 6.01(1)(d) or (1)(e), the expenses (including the reasonable fees and expenses of its counsel) and the compensation for services in connection therewith are to constitute expenses of administration under any bankruptcy law. The provisions of this Section 7.06 shall survive the termination of this Indenture and the resignation or removal of the Trustee.

Section 7.07 Reliance on Officer's Certificate.

Except as otherwise provided in Section 7.01, whenever in the administration of the provisions of this Indenture the Trustee shall deem it reasonably necessary or desirable that a matter be proved or established prior to taking or suffering or omitting to take any action hereunder, such matter (unless other evidence in respect thereof be herein specifically prescribed) may, in the absence of negligence or bad faith on the part of the Trustee, be deemed to be conclusively proved and established by an Officer's Certificate delivered to the Trustee and such certificate, in the absence of negligence or bad faith on the part of the Trustee, shall be full warrant to the Trustee for any action taken, suffered or omitted to be taken by it under the provisions of this Indenture upon the faith thereof.

Section 7.08 Disqualification; Conflicting Interests.

If the Trustee has or shall acquire any "conflicting interest" within the meaning of Section 310(b) of the Trust Indenture Act, the Trustee and the Company shall in all respects comply with the provisions of Section 310(b) of the Trust Indenture Act.

Section 7.09 Corporate Trustee Required; Eligibility.

There shall at all times be a Trustee with respect to the Securities issued hereunder which shall at all times be a corporation organized and doing business under the laws of the United States of America or any state or territory thereof or of the District of Columbia, or a corporation or other Person permitted to act as trustee by the Commission, authorized under such laws to exercise corporate trust powers, having a combined capital and surplus of at least fifty million U.S. dollars ($50,000,000), and subject to supervision or examination by federal, state, territorial, or District of Columbia authority.

If such corporation or other Person publishes reports of condition at least annually, pursuant to law or to the requirements of the aforesaid supervising or examining authority, then for the purposes of this Section, the combined capital and surplus of such corporation or other Person shall be deemed to be its combined capital and surplus as set forth in its most recent report of condition so published. The Company may not, nor may any Person directly or indirectly controlling, controlled by, or under common control with the Company, serve as Trustee. In case at any time the Trustee shall cease to be eligible in accordance with the provisions of this Section, the Trustee shall resign immediately in the manner and with the effect specified in Section 7.10.

Section 7.10 Resignation and Removal; Appointment of Successor.

(1) The Trustee or any successor hereafter appointed may at any time resign with respect to the Securities of one or more series by giving written notice thereof to the Company and by transmitting notice of resignation by mail, first class postage prepaid, to the Securityholders of such series, as their names and addresses appear upon the Security Register. Upon receiving such notice of resignation, the Company shall promptly appoint a successor trustee with respect to Securities of such series by written instrument, in duplicate, executed by order of the Board of Directors, one copy of which instrument shall be delivered to the resigning Trustee and one copy to the successor trustee. If no successor trustee shall have been so appointed and have accepted appointment within 30 days after the mailing of such notice of resignation, the resigning Trustee may petition any court of competent jurisdiction for the appointment of a successor trustee with respect to Securities of such series, or any Securityholder of that series who has been a bona fide holder of a Security or Securities for at least six months may on behalf of himself and all others similarly situated, petition any such court for the appointment of a successor trustee. Such court may thereupon after such notice, if any, as it may deem proper and prescribe, appoint a successor trustee.

(2) In case at any time any one of the following shall occur:

(a) the Trustee shall fail to comply with the provisions of Section 7.08 after written request therefor by the Company or by any Securityholder who has been a bona fide holder of a Security or Securities for at least six months; or

(b) the Trustee shall cease to be eligible in accordance with the provisions of Section 7.09 and shall fail to resign after written request therefor by the Company or by any such Securityholder; or

(c) the Trustee shall become incapable of acting, or shall be adjudged a bankrupt or insolvent, or commence a voluntary bankruptcy proceeding, or a receiver of the Trustee or of its property shall be appointed or consented to, or any public officer shall take charge or control of the Trustee or of its property or affairs for the purpose of rehabilitation, conservation or liquidation;

then, in any such case, the Company may remove the Trustee with respect to all Securities and appoint a successor trustee by written instrument, in duplicate, executed by order of the Board of Directors, one

copy of which instrument shall be delivered to the Trustee so removed and one copy to the successor trustee, or any Securityholder who has been a bona fide holder of a Security or Securities for at least six months may, on behalf of that holder and all others similarly situated, petition any court of competent jurisdiction for the removal of the Trustee and the appointment of a successor trustee. Such court may thereupon after such notice, if any, as it may deem proper and prescribe, remove the Trustee and appoint a successor trustee.

(3) The holders of a majority in aggregate principal amount of the Securities of any series at the time Outstanding may at any time remove the Trustee with respect to such series by so notifying the Trustee and the Company and may appoint a successor Trustee for such series with the consent of the Company.

(4) Any resignation or removal of the Trustee and appointment of a successor trustee with respect to the Securities of a series pursuant to any of the provisions of this Section shall become effective upon acceptance of appointment by the successor trustee as provided in Section 7.11.

(5) Any successor trustee appointed pursuant to this Section may be appointed with respect to the Securities of one or more series or all of such series, and at any time there shall be only one Trustee with respect to the Securities of any particular series.

Section 7.11 Acceptance of Appointment By Successor.

(1) In case of the appointment hereunder of a successor trustee with respect to all Securities, every such successor trustee so appointed shall execute, acknowledge and deliver to the Company and to the retiring Trustee an instrument accepting such appointment, and thereupon the resignation or removal of the retiring Trustee shall become effective and such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, trusts and duties of the retiring Trustee; but, on the request of the Company or the successor trustee, such retiring Trustee shall, upon payment of its charges, execute and deliver an instrument transferring to such successor trustee all the rights, powers, and trusts of the retiring Trustee and shall duly assign, transfer and deliver to such successor trustee all property and money held by such retiring Trustee hereunder.

(2) In case of the appointment hereunder of a successor trustee with respect to the Securities of one or more (but not all) series, the Company, the retiring Trustee and each successor trustee with respect to the Securities of one or more series shall execute and deliver an indenture supplemental hereto wherein each successor trustee shall accept such appointment and which (i) shall contain such provisions as shall be necessary or desirable to transfer and confirm to, and to vest in, each successor trustee all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series to which the appointment of such successor trustee relates, (ii) shall contain such provisions as shall be deemed necessary or desirable to confirm that all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series as to which the retiring Trustee is not retiring shall continue to be vested in the retiring Trustee, and (iii) shall add to or change any of the provisions of this Indenture as shall be necessary to provide for or facilitate the administration of the trusts hereunder by more than one Trustee, it being understood that nothing herein or in such supplemental indenture shall constitute such Trustees co-trustees of the same trust, that each such Trustee shall be trustee of a trust or trusts hereunder separate and apart from any trust or trusts hereunder administered by any other such Trustee and that no Trustee shall be responsible for any act or failure to act on the part of any other Trustee hereunder; and upon the execution and delivery of such supplemental indenture the resignation or removal of the retiring Trustee shall become effective to the extent provided therein, such retiring Trustee shall with respect to the Securities of that or those series to which the appointment of such successor trustee relates have no further responsibility for the exercise of rights and powers or for the performance of the duties and obligations vested in the Trustee under this Indenture, and each such successor trustee, without any further act, deed or conveyance, shall become vested with all the rights, powers, trusts and duties of the retiring Trustee with respect to the Securities of that or those series to which the appointment of such successor trustee relates; but, on request of the Company or any successor trustee, such retiring Trustee shall duly assign, transfer and deliver to such successor trustee, to the extent contemplated by such supplemental indenture, the property and money held by such retiring Trustee hereunder with respect to the Securities of that or those series to which the appointment of such successor trustee relates.

(3) Upon request of any such successor trustee, the Company shall execute any and all instruments for more fully and certainly vesting in and confirming to such successor trustee all such rights, powers and trusts referred to in paragraph (a) or (b) of this Section, as the case may be.

(4) No successor trustee shall accept its appointment unless at the time of such acceptance such successor trustee shall be qualified and eligible under this Article.

(5) Upon acceptance of appointment by a successor trustee as provided in this Section, the Company shall transmit notice of the succession of such trustee hereunder by mail, first class postage prepaid, to the Securityholders, as their names and addresses appear upon the Security Register. If the Company fails to transmit such notice within ten days after acceptance of appointment by the successor trustee, the successor trustee shall cause such notice to be transmitted at the expense of the Company.

Section 7.12 Merger, Conversion, Consolidation or Succession to Business.

Any corporation into which the Trustee may be merged or converted or with which it may be consolidated, or any corporation resulting from any merger, conversion or consolidation to which the Trustee shall be a party, or any corporation succeeding to the corporate trust business of the Trustee, including the administration of the trust created by this Indenture, shall be the successor of the Trustee hereunder, *provided* that such corporation shall be qualified under the provisions of Section 7.08 and eligible under the provisions of Section 7.09, without the execution or filing of any paper or any further act on the part of any of the parties hereto, anything herein to the contrary notwithstanding. In case any Securities shall have been authenticated, but not delivered, by the Trustee then in office, any successor by merger, conversion or consolidation to such authenticating Trustee may adopt such authentication and deliver the Securities so authenticated with the same effect as if such successor Trustee had itself authenticated such Securities.

Section 7.13 Preferential Collection of Claims Against the Company.

The Trustee shall comply with Section 311(a) of the Trust Indenture Act, excluding any creditor relationship described in Section 311(b) of the Trust Indenture Act. A Trustee who has resigned or been removed shall be subject to Section 311(a) of the Trust Indenture Act to the extent included therein.

Section 7.14 Notice of Default.

If any Event of Default occurs and is continuing and if such Event of Default is known to a Responsible Officer of the Trustee, the Trustee shall mail to each Securityholder in the manner and to the extent provided in Section 313(c) of the Trust Indenture Act notice of the Event of Default within the earlier of 90 days after it occurs and 30 days after it is known to a Responsible Officer of the Trustee or written notice of it is received by the Trustee, unless such Event of Default has been cured; *provided*, *however*, that, except in the case of a default in the payment of the principal of (or premium, if any) or interest on any Security, the Trustee shall be protected in withholding such notice if and so long as the board of directors, the executive committee or a trust committee of directors and/or Responsible Officers of the Trustee in good faith determine that the withholding of such notice is in the interest of the Securityholders.

ARTICLE 8

CONCERNING THE SECURITYHOLDERS

Section 8.01 Evidence of Action by Securityholders.

Whenever in this Indenture it is provided that the holders of a majority or specified percentage in aggregate principal amount of the Securities of a particular series may take any action (including the making of any demand or request, the giving of any notice, consent or waiver or the taking of any other action), the fact that at the time of taking any such action the holders of such majority or specified percentage of that series have joined therein may be evidenced by any instrument or any number of instruments of similar tenor executed by such holders of Securities of that series in person or by agent or proxy appointed in writing.

If the Company shall solicit from the Securityholders of any series any request, demand, authorization, direction, notice, consent, waiver or other action, the Company may, at its option, as evidenced by an Officer's Certificate, fix in advance a record date for such series for the determination of Securityholders entitled to give such request, demand, authorization, direction, notice, consent, waiver or other action, but the Company shall have no obligation to do so. If such a record date is fixed, such request, demand, authorization, direction, notice, consent, waiver or other action may be given before or after the record date, but only the Securityholders of record at the close of business on the record date shall be deemed to be Securityholders for the purposes of determining whether Securityholders of the requisite proportion of Outstanding Securities of that series have authorized or agreed or consented to such request, demand, authorization, direction, notice, consent, waiver or other action, and for that purpose the Outstanding Securities of that series shall be computed as of the record date; *provided*, *however*, that no such authorization, agreement or consent by such Securityholders on the record date shall be deemed effective unless it shall become effective pursuant to the provisions of this Indenture not later than six months after the record date.

Section 8.02 Proof of Execution by Securityholders.

Subject to the provisions of Section 7.01, proof of the execution of any instrument by a Securityholder (such proof will not require notarization) or his agent or proxy and proof of the holding by any Person of any of the Securities shall be sufficient if made in the following manner:

(1) The fact and date of the execution by any such Person of any instrument may be proved in any reasonable manner acceptable to the Trustee.

(2) The ownership of Securities shall be proved by the Security Register of such Securities or by a certificate of the Security Registrar thereof.

The Trustee may require such additional proof of any matter referred to in this Section as it shall deem necessary.

Section 8.03 Who May be Deemed Owners.

Prior to the due presentment for registration of transfer of any Security, the Company, the Trustee, any paying agent and any Security Registrar may deem and treat the Person in whose name such Security shall be registered upon the books of the Company as the absolute owner of such Security (whether or not such Security shall be overdue and notwithstanding any notice of ownership or writing thereon made by anyone other than the Security Registrar) for the purpose of receiving payment of or on account of the principal of, premium, if any, and (subject to Section 2.03) interest on such Security and for all other purposes; and neither the Company nor the Trustee nor any paying agent nor any Security Registrar shall be affected by any notice to the contrary.

Section 8.04 Certain Securities Owned by Company Disregarded.

In determining whether the holders of the requisite aggregate principal amount of Securities of a particular series have concurred in any direction, consent or waiver under this Indenture, the Securities of that series that are owned by the Company or any other obligor on the Securities of that series or by any Person directly or indirectly controlling or controlled by or under common control with the Company or any other obligor on the Securities of that series shall be disregarded and deemed not to be Outstanding for the purpose of any such determination, except that for the purpose of determining whether the Trustee shall be protected in relying on any such direction, consent or waiver, only Securities of such series that the Trustee actually knows are so owned shall be so disregarded. The Securities so owned that have been pledged in good faith may be regarded as Outstanding for the purposes of this Section, if the pledgee shall establish to the satisfaction of the Trustee the pledgee's right so to act with respect to such Securities and that the pledgee is not a Person directly or indirectly controlling or controlled by or under direct or indirect common control with the Company or any such other obligor. In case of a dispute as to such right, any decision by the Trustee taken upon the advice of counsel shall be full protection to the Trustee.

Section 8.05 Actions Binding on Future Securityholders.

At any time prior to (but not after) the evidencing to the Trustee, as provided in Section 8.01, of the taking of any action by the holders of the majority or percentage in aggregate principal amount of the Securities of a

particular series specified in this Indenture in connection with such action, any holder of a Security of that series that is shown by the evidence to be included in the Securities the holders of which have consented to such action may, by filing written notice with the Trustee, and upon proof of holding as provided in Section 8.02, revoke such action so far as concerns such Security. Except as aforesaid any such action taken by the holder of any Security shall be conclusive and binding upon such holder and upon all future holders and owners of such Security, and of any Security issued in exchange therefor, on registration of transfer thereof or in place thereof, irrespective of whether or not any notation in regard thereto is made upon such Security. Any action taken by the holders of the majority or percentage in aggregate principal amount of the Securities of a particular series specified in this Indenture in connection with such action shall be conclusively binding upon the Company, the Trustee and the holders of all the Securities of that series.

ARTICLE 9

SUPPLEMENTAL INDENTURES

Section 9.01 Supplemental Indentures Without the Consent of Securityholders.

In addition to any supplemental indenture otherwise authorized by this Indenture, the Company and the Trustee may from time to time and at any time enter into an indenture or indentures supplemental hereto (which shall conform to the provisions of the Trust Indenture Act as then in effect), without the consent of the Securityholders, for one or more of the following purposes:

(1) to cure any ambiguity, defect, or inconsistency herein or in the Securities of any series;

(2) to comply with Article Ten;

(3) to provide for uncertificated Securities in addition to or in place of certificated Securities;

(4) to add to the covenants, restrictions, conditions or provisions relating to the Company for the benefit of the holders of all or any series of Securities (and if such covenants, restrictions, conditions or provisions are to be for the benefit of less than all series of Securities, stating that such covenants, restrictions, conditions or provisions are expressly being included solely for the benefit of such series), to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an Event of Default, or to surrender any right or power herein conferred upon the Company;

(5) to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication, and delivery of Securities, as herein set forth;

(6) to make any change that does not adversely affect the rights of any Securityholder in any material respect;

(7) to provide for the issuance of and establish the form and terms and conditions of the Securities of any series as provided in Section 2.01, to establish the form of any certifications required to be furnished pursuant to the terms of this Indenture or any series of Securities, or to add to the rights of the holders of any series of Securities;

(8) to evidence and provide for the acceptance of appointment hereunder by a successor trustee; or

(9) to comply with any requirements of the Commission or any successor in connection with the qualification of this Indenture under the Trust Indenture Act.

The Trustee is hereby authorized to join with the Company in the execution of any such supplemental indenture, and to make any further appropriate agreements and stipulations that may be therein contained, but the Trustee shall not be obligated to enter into any such supplemental indenture that affects the Trustee's own rights, duties or immunities under this Indenture or otherwise.

Any supplemental indenture authorized by the provisions of this Section may be executed by the Company and the Trustee without the consent of the holders of any of the Securities at the time Outstanding, notwithstanding any of the provisions of Section 9.02.

Section 9.02 Supplemental Indentures With Consent of Securityholders.

With the consent (evidenced as provided in Section 8.01) of the holders of not less than a majority in aggregate principal amount of the Securities of each series affected by such supplemental indenture or indentures at the time Outstanding, the Company, when authorized by a Board Resolution, and the Trustee may from time to time and at any time enter into an indenture or indentures supplemental hereto (which shall conform to the provisions of the Trust Indenture Act as then in effect) for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of this Indenture or of any supplemental indenture or of modifying in any manner not covered by Section 9.01 the rights of the holders of the Securities of such series under this Indenture; *provided, however*, that no such supplemental indenture shall, without the consent of the holders of each Security then Outstanding and affected thereby, (a) extend the fixed maturity of any Securities of any series, or reduce the principal amount thereof, or reduce the rate or extend the time of payment of interest thereon, or reduce any premium payable upon the redemption thereof or (b) reduce the aforesaid percentage of Securities, the holders of which are required to consent to any such supplemental indenture.

It shall not be necessary for the consent of the Securityholders of any series affected thereby under this Section to approve the particular form of any proposed supplemental indenture, but it shall be sufficient if such consent shall approve the substance thereof.

Section 9.03 Effect of Supplemental Indentures.

Upon the execution of any supplemental indenture pursuant to the provisions of this Article or of Section 10.01, this Indenture shall, with respect to such series, be and be deemed to be modified and amended in accordance therewith and the respective rights, limitations of rights, obligations, duties and immunities under this Indenture of the Trustee, the Company and the holders of Securities of the series affected thereby shall thereafter be determined, exercised and enforced hereunder subject in all respects to such modifications and amendments, and all the terms and conditions of any such supplemental indenture shall be and be deemed to be part of the terms and conditions of this Indenture for any and all purposes.

Section 9.04 Securities Affected by Supplemental Indentures.

Securities of any series affected by a supplemental indenture, authenticated and delivered after the execution of such supplemental indenture pursuant to the provisions of this Article or of Section 10.01, may bear a notation in form approved by the Company, provided such form meets the requirements of any securities exchange upon which such series may be listed, as to any matter provided for in such supplemental indenture. If the Company shall so determine, new Securities of that series so modified as to conform, in the opinion of the Board of Directors, to any modification of this Indenture contained in any such supplemental indenture may be prepared by the Company, authenticated by the Trustee and delivered in exchange for the Securities of that series then Outstanding.

Section 9.05 Execution of Supplemental Indentures.

Upon the request of the Company, accompanied by its Board Resolutions authorizing the execution of any such supplemental indenture, and upon the filing with the Trustee of evidence of the consent of Securityholders required to consent thereto as aforesaid, the Trustee shall join with the Company in the execution of such supplemental indenture unless such supplemental indenture affects the Trustee's own rights, duties or immunities under this Indenture or otherwise, in which case the Trustee may in its discretion but shall not be obligated to enter into such supplemental indenture. The Trustee, subject to the provisions of Section 7.01, shall receive an Officer's

Certificate or an Opinion of Counsel as conclusive evidence that any supplemental indenture executed pursuant to this Article is authorized or permitted by the terms of this Article and that all conditions precedent to the execution of the supplemental indenture have been complied with; *provided*, *however*, that such Officer's Certificate or Opinion of Counsel need not be provided in connection with the execution of a supplemental indenture that establishes the terms of a series of Securities pursuant to Section 2.01 hereof.

Promptly after the execution by the Company and the Trustee of any supplemental indenture pursuant to the provisions of this Section, the Company shall (or shall direct the Trustee to) transmit by mail, first class postage prepaid, a notice, setting forth in general terms the substance of such supplemental indenture, to the Securityholders of all series affected thereby as their names and addresses appear upon the Security Register. Any failure of the Company to mail, or cause the mailing of, such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such supplemental indenture.

ARTICLE 10

SUCCESSOR ENTITY

Section 10.01 Company May Consolidate, Etc.

Nothing contained in this Indenture shall prevent any consolidation or merger of the Company with or into any other Person (whether or not affiliated with the Company) or successive consolidations or mergers in which the Company or its successor or successors shall be a party or parties, or shall prevent any sale, conveyance, transfer or other disposition of the property of the Company or its successor or successors as an entirety, or substantially as an entirety, to any other corporation (whether or not affiliated with the Company or its successor or successors) authorized to acquire and operate the same; *provided*, *however*, (a) the Company hereby covenants and agrees that, upon any such consolidation or merger (in each case, if the Company is not the survivor of such transaction), sale, conveyance, transfer or other disposition, the due and punctual payment of the principal of (premium, if any) and interest on all of the Securities of all series in accordance with the terms of each series, according to their tenor, and the due and punctual performance and observance of all the covenants and conditions of this Indenture with respect to each series or established with respect to such series pursuant to Section 2.01 to be kept or performed by the Company shall be expressly assumed, by supplemental indenture (which shall conform to the provisions of the Trust Indenture Act, as then in effect) reasonably satisfactory in form to the Trustee executed and delivered to the Trustee by the entity formed by such consolidation, or into which the Company shall have been merged, or by the entity which shall have acquired such property and (b) in the event that the Securities of any series then Outstanding are convertible into or exchangeable for shares of common stock or other securities of the Company, such entity shall, by such supplemental indenture, make provision so that the Securityholders of Securities of that series shall thereafter be entitled to receive upon conversion or exchange of such Securities the number of securities or property to which a holder of the number of shares of common stock or other securities of the Company deliverable upon conversion or exchange of those Securities would have been entitled had such conversion or exchange occurred immediately prior to such consolidation, merger, sale, conveyance, transfer or other disposition.

Section 10.02 Successor Entity Substituted.

(1) In case of any such consolidation, merger, sale, conveyance, transfer or other disposition and upon the assumption by the successor entity by supplemental indenture, executed and delivered to the Trustee and satisfactory in form to the Trustee, of the obligations set forth under Section 10.01 on all of the Securities of all series Outstanding, such successor entity shall succeed to and be substituted for the Company with the same effect as if it had been named as the Company herein, and thereupon the predecessor corporation shall be relieved of all obligations and covenants under this Indenture and the Securities.

(2) In case of any such consolidation, merger, sale, conveyance, transfer or other disposition, such changes in phraseology and form (but not in substance) may be made in the Securities thereafter to be issued as may be appropriate.

(3) Nothing contained in this Article shall require any action by the Company in the case of a consolidation or merger of any Person into the Company where the Company is the survivor of such transaction, or the acquisition by the Company, by purchase or otherwise, of all or any part of the property of any other Person (whether or not affiliated with the Company).

ARTICLE 11

SATISFACTION AND DISCHARGE

Section 11.01 Satisfaction and Discharge of Indenture.

If at any time: (a) the Company shall have delivered to the Trustee for cancellation all Securities of a series theretofore authenticated and not delivered to the Trustee for cancellation (other than any Securities that shall have been destroyed, lost or stolen and that shall have been replaced or paid as provided in Section 2.07 and Securities for whose payment money or Governmental Obligations have theretofore been deposited in trust or segregated and held in trust by the Company and thereupon repaid to the Company or discharged from such trust, as provided in Section 11.05); or (b) all such Securities of a particular series not theretofore delivered to the Trustee for cancellation shall have become due and payable, or are by their terms to become due and payable within one year or are to be called for redemption within one year under arrangements satisfactory to the Trustee for the giving of notice of redemption, and the Company shall deposit or cause to be deposited with the Trustee as trust funds the entire amount in moneys or Governmental Obligations or a combination thereof, sufficient in the opinion of a nationally recognized firm of independent public accountants expressed in a written certification thereof delivered to the Trustee, to pay at maturity or upon redemption all Securities of that series not theretofore delivered to the Trustee for cancellation, including principal (and premium, if any) and interest due or to become due to such date of maturity or date fixed for redemption, as the case may be, and if the Company shall also pay or cause to be paid all other sums payable hereunder with respect to such series by the Company then this Indenture shall thereupon cease to be of further effect with respect to such series except for the provisions of Sections 2.03, 2.05, 2.07, 4.01, 4.02, 4.03 and 7.10, that shall survive until the date of maturity or redemption date, as the case may be, and Sections 7.06 and 11.05, that shall survive to such date and thereafter, and the Trustee, on demand of the Company and at the cost and expense of the Company shall execute proper instruments acknowledging satisfaction of and discharging this Indenture with respect to such series.

Section 11.02 Discharge of Obligations.

If at any time all such Securities of a particular series not heretofore delivered to the Trustee for cancellation or that have not become due and payable as described in Section 11.01 shall have been paid by the Company by depositing irrevocably with the Trustee as trust funds moneys or an amount of Governmental Obligations sufficient to pay at maturity or upon redemption all such Securities of that series not theretofore delivered to the Trustee for cancellation, including principal (and premium, if any) and interest due or to become due to such date of maturity or date fixed for redemption, as the case may be, and if the Company shall also pay or cause to be paid all other sums payable hereunder by the Company with respect to such series, then after the date such moneys or Governmental Obligations, as the case may be, are deposited with the Trustee the obligations of the Company under this Indenture with respect to such series shall cease to be of further effect except for the provisions of Sections 2.03, 2.05, 2.07, 4.01, 4.02, 4.03, 7.06, 7.10 and 11.05 hereof that shall survive until such Securities shall mature and be paid.

Thereafter, Sections 7.06 and 11.05 shall survive.

Section 11.03 Deposited Moneys to be Held in Trust.

All moneys or Governmental Obligations deposited with the Trustee pursuant to Sections 11.01 or 11.02 shall be held in trust and shall be available for payment as due, either directly or through any paying agent (including the Company acting as its own paying agent), to the holders of the particular series of Securities for the payment or redemption of which such moneys or Governmental Obligations have been deposited with the Trustee.

Section 11.04 Payment of Moneys Held by Paying Agents.

In connection with the satisfaction and discharge of this Indenture all moneys or Governmental Obligations then held by any paying agent under the provisions of this Indenture shall, upon demand of the Company, be paid to the Trustee and thereupon such paying agent shall be released from all further liability with respect to such moneys or Governmental Obligations.

Section 11.05 Repayment to Company.

Any moneys or Governmental Obligations deposited with any paying agent or the Trustee, or then held by the Company, in trust for payment of principal of or premium, if any, or interest on the Securities of a particular series that are not applied but remain unclaimed by the holders of such Securities for at least two years after the date upon which the principal of (and premium, if any) or interest on such Securities shall have respectively become due and payable, or such other shorter period set forth in applicable escheat or abandoned or unclaimed property law, shall be repaid to the Company on May 31 of each year or upon the Company's request or (if then held by the Company) shall be discharged from such trust; and thereupon the paying agent and the Trustee shall be released from all further liability with respect to such moneys or Governmental Obligations, and the holder of any of the Securities entitled to receive such payment shall thereafter, as a general creditor, look only to the Company for the payment thereof.

ARTICLE 12

IMMUNITY OF INCORPORATORS, STOCKHOLDERS, OFFICERS AND DIRECTORS

Section 12.01 No Recourse.

No recourse under or upon any obligation, covenant or agreement of this Indenture, or of any Security, or for any claim based thereon or otherwise in respect thereof, shall be had against any incorporator, stockholder, officer or director, past, present or future as such, of the Company or of any predecessor or successor corporation, either directly or through the Company or any such predecessor or successor corporation, whether by virtue of any constitution, statute or rule of law, or by the enforcement of any assessment or penalty or otherwise; it being expressly understood that this Indenture and the obligations issued hereunder are solely corporate obligations, and that no such personal liability whatever shall attach to, or is or shall be incurred by, the incorporators, stockholders, officers or directors as such, of the Company or of any predecessor or successor corporation, or any of them, because of the creation of the indebtedness hereby authorized, or under or by reason of the obligations, covenants or agreements contained in this Indenture or in any of the Securities or implied therefrom; and that any and all such personal liability of every name and nature, either at common law or in equity or by constitution or statute, of, and any and all such rights and claims against, every such incorporator, stockholder, officer or director as such, because of the creation of the indebtedness hereby authorized, or under or by reason of the obligations, covenants or agreements contained in this Indenture or in any of the Securities or implied therefrom, are hereby expressly waived and released as a condition of, and as a consideration for, the execution of this Indenture and the issuance of such Securities.

ARTICLE 13

MISCELLANEOUS PROVISIONS

Section 13.01 Effect on Successors and Assigns.

All the covenants, stipulations, promises and agreements in this Indenture made by or on behalf of the Company shall bind its successors and assigns, whether so expressed or not.

Section 13.02 Actions by Successor.

Any act or proceeding by any provision of this Indenture authorized or required to be done or performed by any board, committee or officer of the Company shall and may be done and performed with like force and effect by the corresponding board, committee or officer of any corporation that shall at the time be the lawful successor of the Company.

Section 13.03 Surrender of Company Powers.

The Company by instrument in writing executed by authority of its Board of Directors and delivered to the Trustee may surrender any of the powers reserved to the Company, and thereupon such power so surrendered shall terminate both as to the Company and as to any successor corporation.

Section 13.04 Notices.

Except as otherwise expressly provided herein, any notice, request or demand that by any provision of this Indenture is required or permitted to be given, made or served by the Trustee or by the holders of Securities or by any other Person pursuant to this Indenture to or on the Company may be given or served by being deposited in first class mail, postage prepaid, addressed (until another address is filed in writing by the Company with the Trustee), as follows: . Any notice, election, request or demand by the Company or any Securityholder or by any other Person pursuant to this Indenture to or upon the Trustee shall be deemed to have been sufficiently given or made, for all purposes, if given or made in writing at the Corporate Trust Office of the Trustee.

Section 13.05 Governing Law.

This Indenture and each Security shall be deemed to be a contract made under the internal laws of the State of New York, and for all purposes shall be construed in accordance with the laws of said State, except to the extent that the Trust Indenture Act is applicable.

Section 13.06 Treatment of Securities as Debt.

It is intended that the Securities will be treated as indebtedness and not as equity for federal income tax purposes. The provisions of this Indenture shall be interpreted to further this intention.

Section 13.07 Certificates and Opinions as to Conditions Precedent.

(1) Upon any application or demand by the Company to the Trustee to take any action under any of the provisions of this Indenture, the Company shall furnish to the Trustee an Officer's Certificate stating that all conditions precedent provided for in this Indenture (other than the certificate to be delivered pursuant to Section 13.12) relating to the proposed action have been complied with and, if requested, an Opinion of Counsel stating that in the opinion of such counsel all such conditions precedent have been complied with, except that in the case of any such application or demand as to which the furnishing of such documents is specifically required by any provision of this Indenture relating to such particular application or demand, no additional certificate or opinion need be furnished.

(2) Each certificate or opinion provided for in this Indenture and delivered to the Trustee with respect to compliance with a condition or covenant in this Indenture shall include (i) a statement that the Person making such certificate or opinion has read such covenant or condition; (ii) a brief statement as to the nature and scope of the examination or investigation upon which the statements or opinions contained in such certificate or opinion are based; (iii) a statement that, in the opinion of such Person, he has made such examination or investigation as is reasonably necessary to enable him to express an informed opinion as to whether or not such covenant or condition has been complied with; and (iv) a statement as to whether or not, in the opinion of such Person, such condition or covenant has been complied with.

Section 13.08 Payments on Business Days.

Except as provided pursuant to Section 2.01 pursuant to a Board Resolution, and set forth in an Officer's Certificate, or established in one or more indentures supplemental to this Indenture, in any case where the date of maturity of interest or principal of any Security or the date of redemption of any Security shall not be a Business Day, then payment of interest or principal (and premium, if any) may be made on the next succeeding Business Day with the same force and effect as if made on the nominal date of maturity or redemption, and no interest shall accrue for the period after such nominal date.

Section 13.09 Conflict with Trust Indenture Act.

If and to the extent that any provision of this Indenture limits, qualifies or conflicts with the duties imposed by Sections 310 to 317, inclusive, of the Trust Indenture Act, such imposed duties shall control.

Section 13.10 Counterparts.

This Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument.

Section 13.11 Separability.

In case any one or more of the provisions contained in this Indenture or in the Securities of any series shall for any reason be held to be invalid, illegal or unenforceable in any respect, such invalidity, illegality or unenforceability shall not affect any other provisions of this Indenture or of such Securities, but this Indenture and such Securities shall be construed as if such invalid or illegal or unenforceable provision had never been contained herein or therein.

Section 13.12 Compliance Certificates.

The Company shall deliver to the Trustee, within 120 days after the end of each fiscal year during which any Securities of any series were outstanding, an officer's certificate stating whether or not the signers know of any Event of Default that occurred during such fiscal year. Such certificate shall contain a certification from the principal executive officer, principal financial officer or principal accounting officer of the Company that a review has been conducted of the activities of the Company and the Company's performance under this Indenture and that the Company has complied with all conditions and covenants under this Indenture. For purposes of this Section 13.12, such compliance shall be determined without regard to any period of grace or requirement of notice provided under this Indenture. If the officer of the Company signing such certificate has knowledge of such an Event of Default, the certificate shall describe any such Event of Default and its status.

IN WITNESS WHEREOF, the parties hereto have caused this Indenture to be duly executed all as of the day and year first above written.

AERPIO PHARMACEUTICALS, INC.

By: _____
Name: _____
Title: _____

AMERICAN STOCK TRANSFER & TRUST COMPANY, LLC, as Trustee

By: _____
Name: _____
Title: _____

CROSS-REFERENCE TABLE (1)

Section of Trust Indenture Act of 1939, as Amended	Section of Indenture
310(a)	7.09
310(b)	7.08
	7.10
310(c)	Inapplicable
311(a)	7.13
311(b)	7.13
311(c)	Inapplicable
312(a)	5.01
	5.02(1)
312(b)	5.02(3)
312(c)	5.02(3)
313(a)	5.04(1)
313(b)	5.04(2)
313(c)	5.04(1)
	5.04(2)
313(d)	5.04(3)
314(a)	5.03
	13.12
314(b)	Inapplicable
314(c)	13.07(1)
314(d)	Inapplicable
314(e)	13.07(2)
314(f)	Inapplicable
315(a)	7.01(1)
	7.01(2)
315(b)	7.14
315(c)	7.01
315(d)	7.01(2)
315(e)	6.07
316(a)	6.06
	8.04
316(b)	6.04
316(c)	8.01
317(a)	6.02
317(b)	4.03
318(a)	13.09

(1) This Cross-Reference Table does not constitute part of the Indenture and shall not have any bearing on the interpretation of any of its terms or provisions.

Exhibit 5.1

February 21, 2018

Aerpio Pharmaceuticals, Inc.
9987 Carver Road
Cincinnati, OH 45242

Re: Securities Being Registered under Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-3 (as amended or supplemented, the "Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration of up to $150,000,000 of any combination of (i) common stock, par value $0.0001 per share (the "Common Stock"), of Aerpio Pharmaceuticals, Inc., a Delaware corporation (the "Company"), (ii) preferred stock, par value $0.0001 per share, of the Company (the "Preferred Stock"), (iii) debt securities of the Company ("Debt Securities"), (iv) warrants to purchase Common Stock, Preferred Stock, Debt Securities or Units (as defined below) ("Warrants"), and (v) units comprised of Common Stock, Preferred Stock, Debt Securities, (as defined below), Warrants and other securities in any combination ("Units"). The Common Stock, Preferred Stock, Debt Securities, Warrants, and Units are sometimes referred to collectively herein as the "Securities." Securities may be issued in an unspecified number (with respect to Common Stock, Preferred Stock, Warrants, and Units) or in an unspecified principal amount (with respect to Debt Securities). The Registration Statement provides that the Securities may be offered separately or together, in separate series, in amounts, at prices and on terms to be set forth in one or more prospectus supplements (each a "Prospectus Supplement") to the prospectus contained in the Registration Statement.

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinions set forth below, on certificates of officers of the Company.

The opinions set forth below are limited to the Delaware General Corporation Law and the laws of the State of New York.

For purposes of the opinions set forth below, without limiting any other exceptions or qualifications set forth herein, we have assumed that after the issuance of any Securities offered pursuant to the Registration Statement, the total number of issued shares of Common Stock or Preferred Stock, as applicable, together with the total number of shares of such stock issuable upon the exercise, exchange, conversion or settlement, as the case may be, of any exercisable, exchangeable or convertible security (including without limitation any Unit), as the case may be, then outstanding, will not exceed the total number of authorized shares of Common Stock or Preferred Stock, as applicable, under the Company's certificate of incorporation as then in effect (the "Charter").

For purposes of the opinions set forth below, we refer to the following as the "Future Authorization and Issuance" of Securities:

- with respect to any of the Securities, (a) the authorization by the Company of the amount, terms and issuance of such Securities (the "Authorization") and (b) the issuance of such Securities in accordance with the Authorization therefor upon the receipt by the Company of the consideration (which, in the case of shares of Common Stock or Preferred Stock, is not less than the par value of such shares) to be paid therefor in accordance with the Authorization;
- with respect to Preferred Stock, (a) the establishment of the terms of such Preferred Stock by the Company in conformity with the Charter and applicable law and (b) the execution, acknowledgement and filing with the Delaware Secretary of State, and the effectiveness of, a certificate of designations to the Charter setting forth the terms of such Preferred Stock in accordance with the Charter and applicable law;
- with respect to Debt Securities, (a) the authorization, execution and delivery of the indenture or a supplemental indenture relating to such Securities by the Company and the trustee thereunder and/or (b) the establishment of the terms of such Securities by the Company in conformity with the applicable indenture or supplemental indenture and applicable law, and (c) the execution, authentication and issuance of such Securities in accordance with the applicable indenture or supplemental indenture and applicable law; and
- with respect to Warrants or Units, (a) the authorization, execution and delivery by the Company and the other parties thereto of any agreement under which such Securities are to be issued and (b) the establishment of the terms of such Securities, and the execution and delivery of such Securities, in conformity with any applicable agreement under which such Securities are to be issued and applicable law.

Based upon the foregoing, and subject to the additional qualifications set forth below, we are of the opinion that:

1. Upon the Future Authorization and Issuance of shares of Common Stock, such shares of Common Stock will be validly issued, fully paid and nonassessable.

2. Upon the Future Authorization and Issuance of shares of Preferred Stock, such shares of Preferred Stock will be validly issued, fully paid and nonassessable.

3. Upon the Future Authorization and Issuance of Debt Securities, such Debt Securities will be valid and binding obligations of the Company.

4. Upon the Future Authorization and Issuance of Warrants, such Warrants will be valid and binding obligations of the Company.

5. Upon the Future Authorization and Issuance of Units, such Units will be valid and binding obligations of the Company.

The opinions expressed above are subject to bankruptcy, insolvency, fraudulent transfer, reorganization, moratorium and other similar laws of general application affecting the rights and remedies of creditors and to general principles of equity.

This opinion letter and the opinions it contains shall be interpreted in accordance with the Legal Opinion Principles issued by the Committee on Legal Opinions of the American Bar Association's Business Law Section as published in 53 Business Lawyer 831 (May 1998).

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the Registration Statement and to the references to our firm under the caption "Legal Matters" in the Registration Statement. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,

/S/ GOODWIN PROCTER LLP

GOODWIN PROCTER LLP

Exhibit 5.2

February 21, 2018

Aerpio Pharmaceuticals, Inc.
9987 Carver Road, Suite 420
Cincinnati, OH 45242

Re: Securities Registered under Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to you in connection with your filing of a Registration Statement on Form S-3 (as amended or supplemented, the "Registration Statement") filed on February 21, 2018 with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration of the offering by Aerpio Pharmaceuticals, Inc., a Delaware corporation (the "Company") of up to $150,000,000 of any combination of securities of the types specified therein. Reference is made to our opinion letter dated February 21, 2018 and included as Exhibit 5.1 to the Registration Statement. We are delivering this supplemental opinion letter in connection with the sales agreement prospectus supplement (the "Prospectus Supplement") contained in the Registration Statement. The Prospectus Supplement relates to the offering by the Company of up to $75,000,000 in shares (the "Shares") of the Company's common stock, par value $0.0001 per share ("Common Stock"), covered by the Registration Statement. The Shares are being offered and sold by the sales agent named in, and pursuant to, the Controlled Equity Offering℠ sales agreement dated February 21, 2018 between the Company and the sales agent.

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinions set forth below, on certificates of officers of the Company.

For purposes of the opinion set forth below, we have assumed that the Shares are issued for a price per share equal to or greater than the minimum price authorized by the Company's board of directors prior to the date hereof (the "Minimum Price") and, in the future, the Company does not issue shares of Common Stock or reduce the total number of shares of Common Stock that the Company is authorized to issue under its certificate of incorporation, as amended, such that the number of authorized but unissued shares of Common Stock under the Company's certificate of incorporation, as amended, is less than the number of unissued Shares that may be issued for the Minimum Price.

For purposes of the opinions set forth below, we refer to the following as "Future Approval and Issuance": (a) the approval by the Company's board of directors (or a duly

authorized committee of the board of directors) of the issuance of the Shares (the "Approval") and (b) the issuance of the Shares in accordance with the Approval and the receipt by the Company of the consideration (which shall not be less than the par value of such Shares) to be paid in accordance with the Approval.

The opinion set forth below is limited to the Delaware General Corporation Law.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized and, upon Future Approval and Issuance, will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion letter as an exhibit to the Registration Statement and the reference to our firm in that report. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,

/s/ Goodwin Procter LLP

GOODWIN PROCTER LLP

Exhibit 12.1

Computation of Ratio of Earnings to Fixed Charges

	Nine Months Ended September 30, 2017	Year Ended December 31, 2016	2015
Fixed Charges:			
Interest expense on indebtedness	$ 246,841	$ 482,204	$ —
Portion of rental expenses which represents interest expense	—	—	—
Total fixed charges	$ 246,841	$ 482,204	$ —
Total earnings available for fixed charges	(4,649,567)	(16,983,511)	(17,070,223)
Deficiency of earnings to fixed charges	$(4,896,408)	$(17,465,715)	$(17,070,223)

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption “Experts” in this Registration Statement (Form S-3) and related Prospectus of Aerpio Pharmaceuticals, Inc. for the registration of common stock, preferred stock, debt securities, warrants, and/or units and to the incorporation by reference therein of our report dated March 9, 2017 (except for the paragraphs included under the caption “Merger and Offering” described in Notes 1 and 15, as to which the date is May 22, 2017), with respect to the consolidated financial statements of Aerpio Pharmaceuticals, Inc., included in its Registration Statement (Form S-1 No. 333-217320) and related Prospectus, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Cincinnati, Ohio
February 21, 2018

Exhibit 23.2

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of Aerpio Pharmaceuticals, Inc. of our report dated March 7, 2017, with respect to our audits of the financial statements of Zeta Acquisition Corp. II for the years ended December 31, 2016 and 2015, which appears in the Zeta Acquisition Corp. II Form 10-K filed on March 7, 2017.

/s/LWBJ, LLP
West Des Moines, Iowa
February 21, 2018