UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2017

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 000-53057

Aerpio Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**EIN 61-1547850**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
9987 Carver Road, Cincinnati, OH	**45242**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (513) 985-1920

Securities registered pursuant to Section 12(b) of the Act: Common Stock, Par Value $0.0001 Per Share; Common stock traded on the over-the-counter market middle tier group, or OTCQB stock market.

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit and post such files). YES ☒ NO ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth 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.

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

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 13(a) of the Exchange Act. ☒

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The registrant's common stock began trading on the OTCQB on August 8, 2017. As of March 8, 2018, the aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold on March 8, 2018 was approximately $77,257,985. The registrant has provided this information as of March 8, 2018 because the registrant's stock was not trading on a national securities exchange as of the last business day of its most recently completed second fiscal quarter and therefore cannot calculate the aggregate market value of its voting and non-voting equity held by non-affiliates as of such date.

As of March 8, 2018, there were 27,140,969 shares of common stock, $0.0001 par value per share, outstanding.

Portions of the Registrant's Definitive Proxy Statement relating to the Annual Meeting of Shareholders are incorporated by reference into Part III of this Report. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of the Registrant's fiscal year ended December 31, 2017.

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Forward-Looking Statements

This Annual Report on Form 10-K contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements may be identified by forward-looking words such as “may,” “could,” “should,” “would,” “will,” “plans,” “intend,” “expect,” “anticipate,” “predicts,” “potential,” “believe,” “continue” or similar words, although not all forward-looking statements contain these identifying words. Forward-looking statements include, but are not limited to, 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.

Readers should not place undue reliance on these forward-looking statements. Our actual results may differ materially from such forward-looking statements as a result of numerous factors, some of which we may not be able to predict and may not be within our control. Factors that could cause such differences include, but are not limited to, the accuracy of our estimates regarding expense, future revenues, uses of cash, capital requirements and the need for additional financing; our ability to continue as a going concern; the initiation, cost, timing, progress and results of our development activities, preclinical studies and clinical trials; the timing of and our ability to obtain and maintain regulatory approval of our existing product candidates, any product candidates that we may develop, and any related restrictions, limitations, and/or warnings in the label of any approved product candidates; our plans to research, develop and commercialize our current and future product candidates; our ability to attract collaborators with development, regulatory and commercialization expertise; our ability to obtain and maintain intellectual property protection for our product candidates; our ability to successfully commercialize our product candidates; the size and growth of the markets for our product candidates and our ability to serve those markets; the success of competing drugs that are or become available; our ability to obtain additional financing; our ability to attract and retain key personnel, as well as those risks discussed elsewhere in this report, including under the heading “Risk Factors.” All forward-looking statements are made as of the date of this report and we do not undertake any obligation to update our forward-looking statements, except as required by applicable law.

PART I

Item 1. 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 stop, slow down or 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. We expect to report top line results of this trial in the second quarter of 2019.

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 Food and Drug Administration, or 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 activity 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 will consider 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 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 146 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 estimated 65-70% 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 and Diabetic Macular Edema 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.

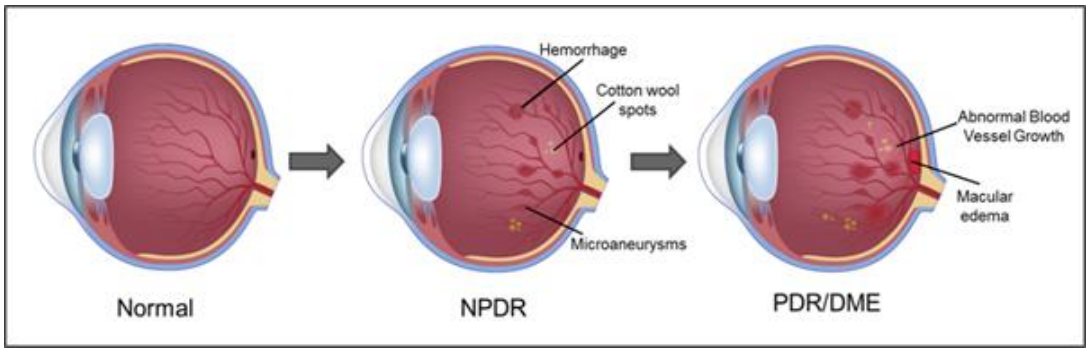


Figure 1: Progression of diabetic eye disease is characterized by worsening vascular compromise.

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.

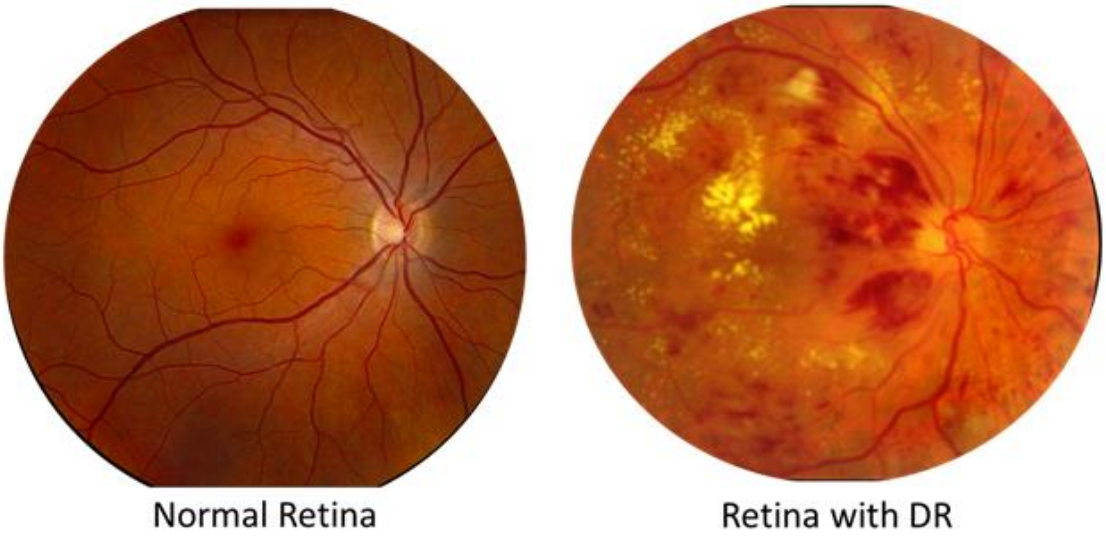


Figure 2. Fundus photographs or a normal retina (left) and a retina with advanced DR (right)

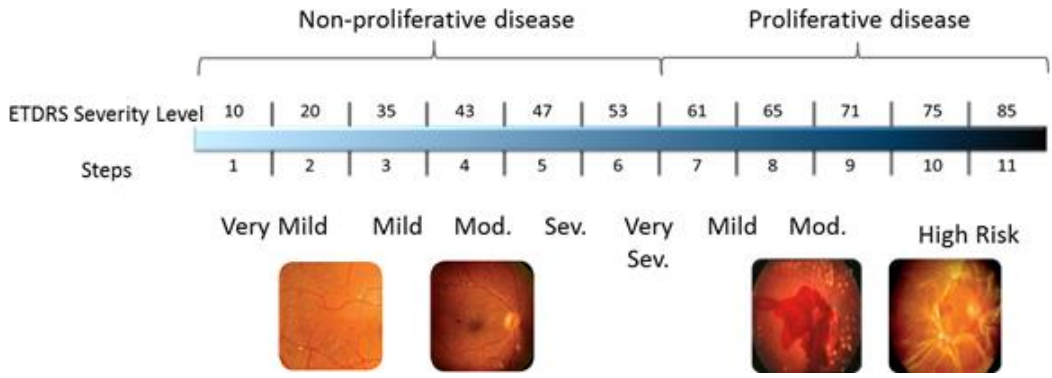


Figure 3: Early Treatment of Diabetic Retinopathy Study scale used to grade fundus images of the retina and measure the progression and regression of diabetic retinopathy.

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

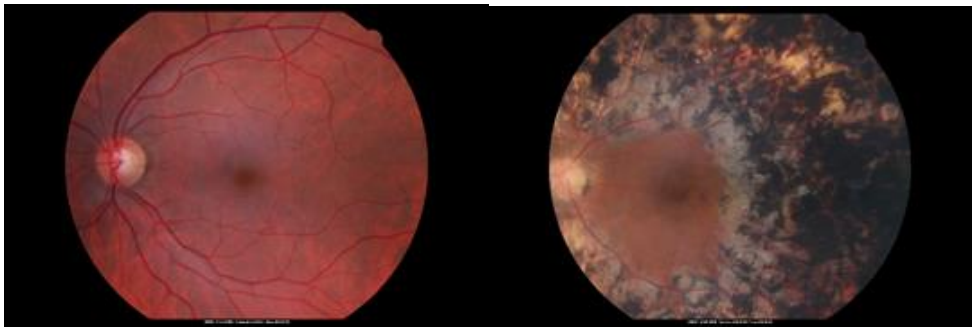


Figure 4: Normal retina (left). Retina after panretinal laser photocoagulation (right).

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 (approximately 70% of DR patients have 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 approximately 65-70% of diabetic eye disease patients have bilateral disease, reduce or slow progression to development of vision-threatening events, such as DME and PDR, and possibly 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, contributes to vascular destabilization.

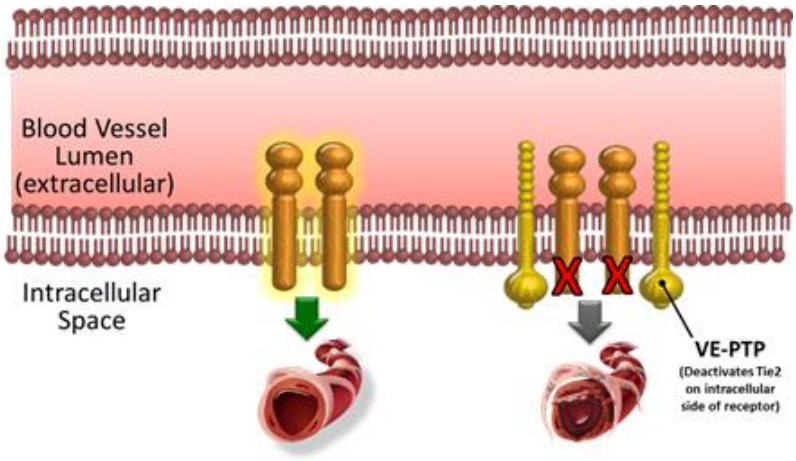


Figure 5. VE-PTP is upregulated in diabetic vasculature and leads to deactivation of the Tie2 receptor

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.

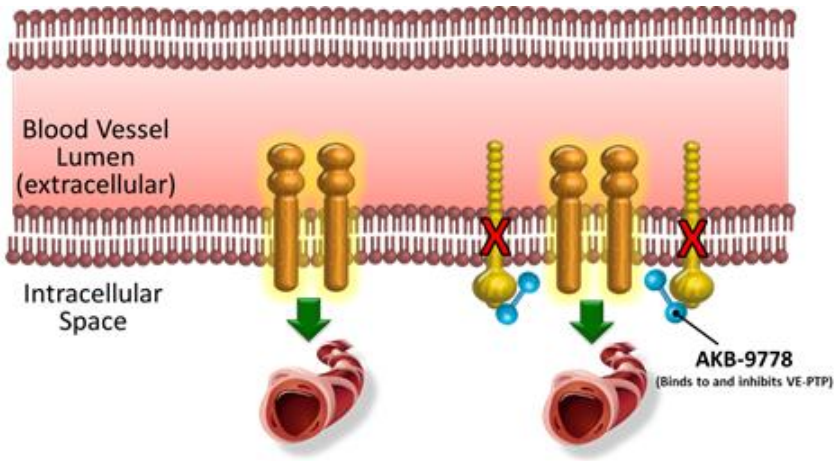


Figure 6. AKB-9778 binds to and inhibits the active site of VE-PTP, resulting in Tie2 activation.

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 (refer to Figure 7).

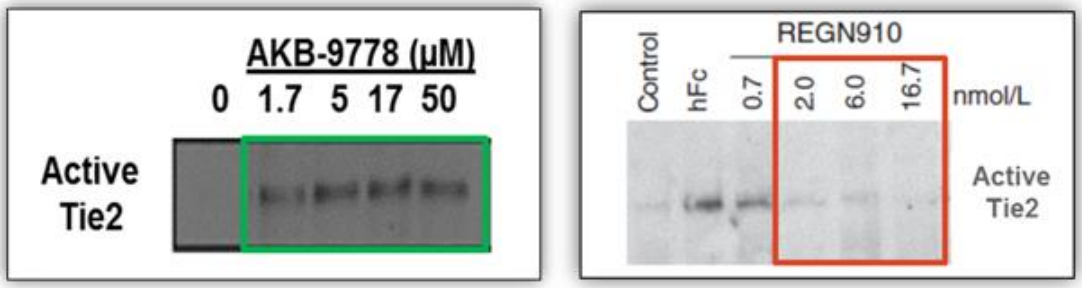


Figure 7. Inhibiting VE-PTP with AKB-9778 robustly activates Tie2 in human endothelial cells in pre-clinical experiments (Shen et al. JCI 124:4564-76, 2014). Ang-2 inhibition, with REGN910 (nesvacumab), results in minimal Tie2 activation in human endothelial cells in pre-clinical experiments (Daly et 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 vascular endothelial growth factor, or VEGF loads. Anti-VEGF therapy is required to reduce the VEGF load and the resultant permeability. In animal models, therapy with AKB-9778 activates the Tie2 receptor, which has been shown to reduce the endothelial response to VEGF and normalize vasculature, improve blood flow and oxygenation potentially leading to reduced VEGF production. These findings explain, in part, why combination therapy may produce greater clinical activity than anti-VEGF alone and provide 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 and PDR.

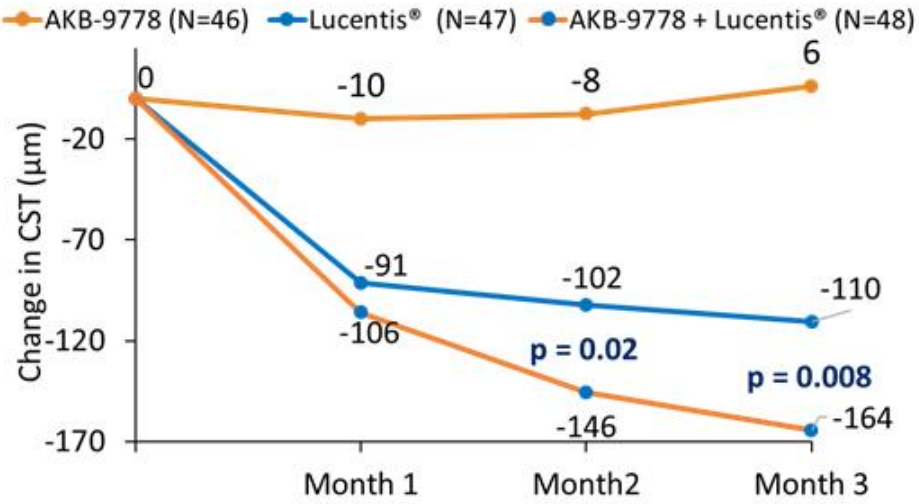


Figure 8. Aggregate Data for Reduction in CST in Phase 2a trial in patients with DME.

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.

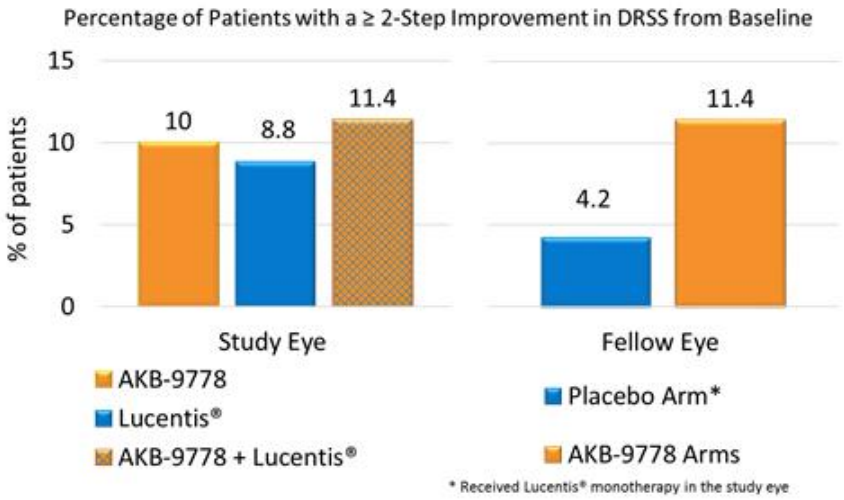


Figure 9. Percent of patients with a 2 or more-step improvement in diabetic retinopathy from baseline to three months in the Phase 2a, TIME-2 trial.

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.

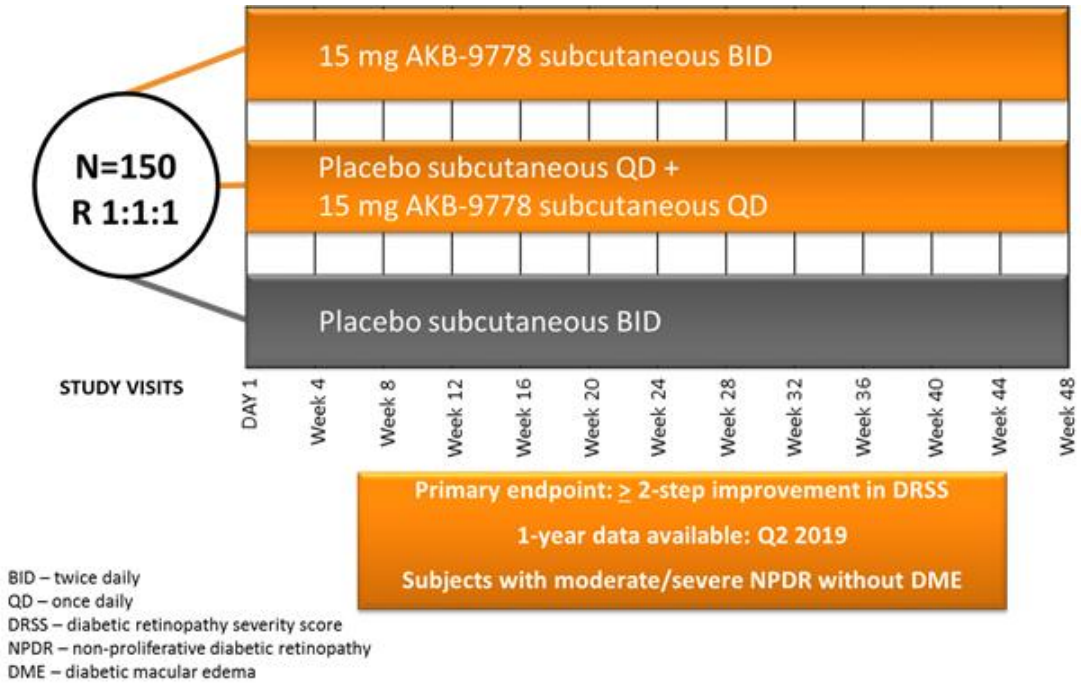


Figure 10. Trial design for Phase 2b trial in DR with AKB-9778

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 (i.e. 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 by previous therapeutic approaches (i.e. Lucentis): 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 compared to intra-vitreal injection: reduction of visit and treatment burden
- Potential ability to benefit disease in both eyes
- Potential ability to benefit other vascular beds
- 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.

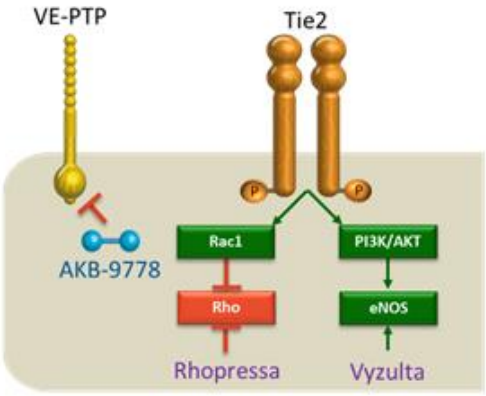


Figure 11. VE-PTP inhibition as a novel conventional outflow targeted approach for glaucoma treatment.

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 β-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 New Zealand White 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 and the treatment was well-tolerated with no visible irritation or hyperemia seen.

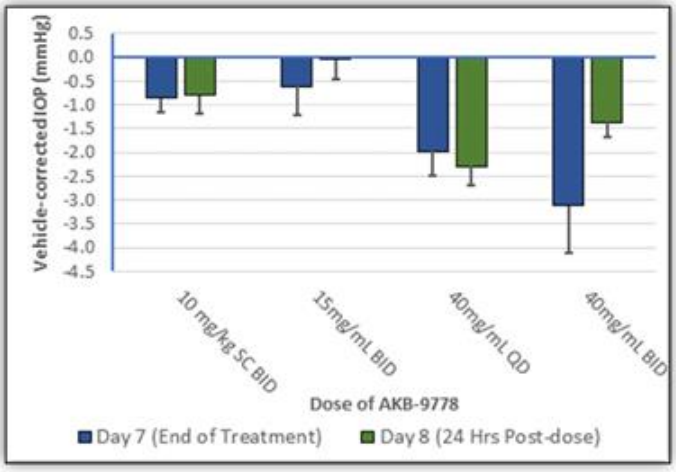


Figure 13. IOP effects of topical ocular compared to subcutaneous AKB-9778 in male rabbits. High dose topical ocular (40 mg/ml) AKB-9778 administered either QD or BID reduced IOP more than low dose topical (15 mg/ml) or subcutaneous (10 mg/kg) administration BID (Day 7). IOP effects persisted 24 hours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

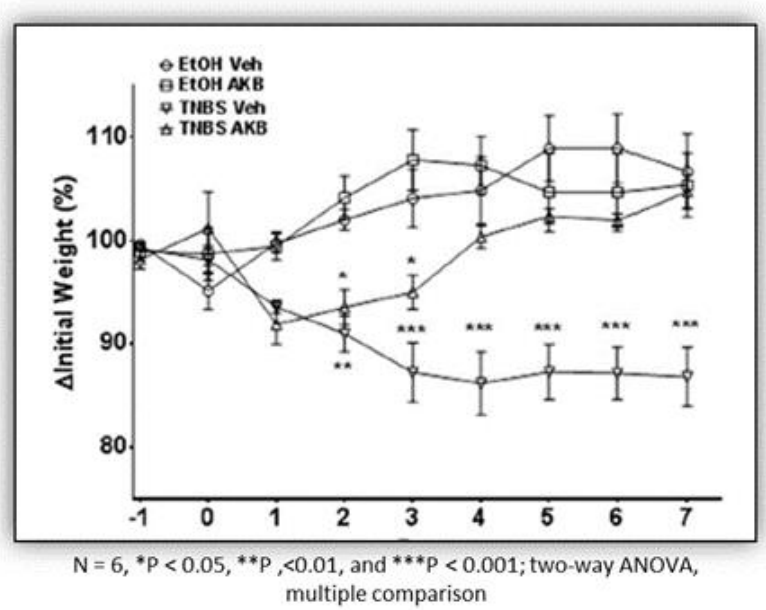


Figure 15. Orally dosed AKB-4924 (5 mg/kg) reverses weight loss induced by trinitrobezenesulfonic acid (TNBS) colitis.

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 ΔARE 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.

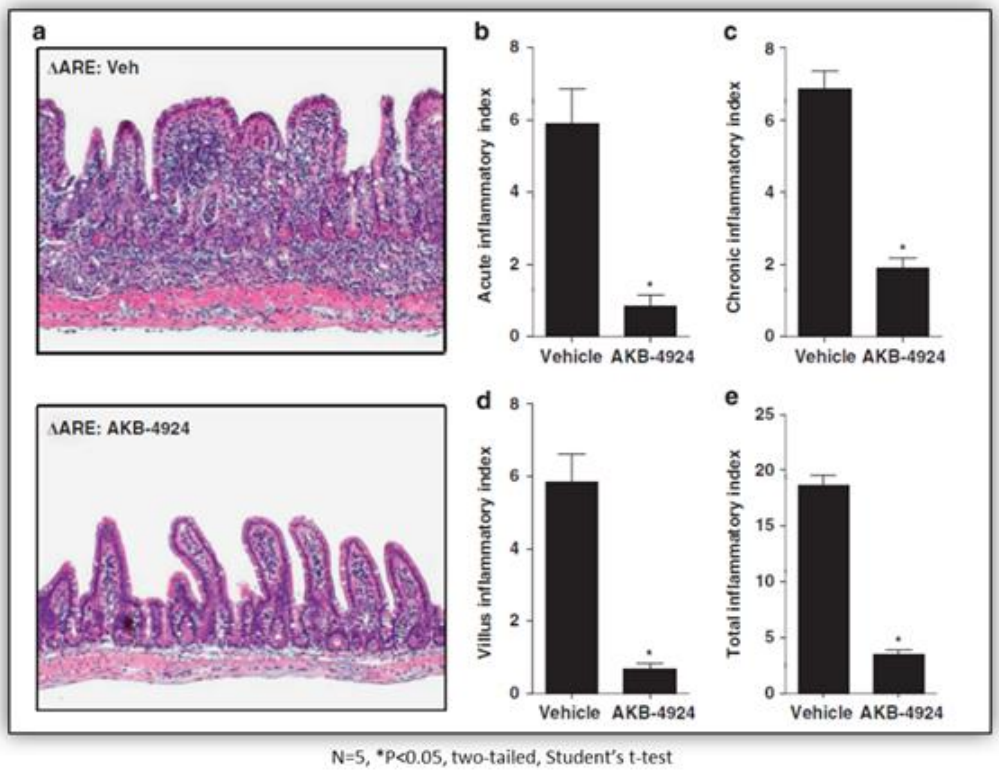


Figure 16. Terminal ileitis in control animals (a-top panel), terminal ileitis was completely reversed via administration of AKB-4924 (a-bottom panel). AKB-4924 administration resulted in a decrease of all inflammatory scores.

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 December 31, 2017, we owned at least 33 U.S. patents, at least 15 pending U.S. provisional or non-provisional patent applications, at least 324 foreign patents, and at least 118 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 December 31, 2017, we owned at least 3 U.S. patents, at least 5 pending U.S. provisional or non-provisional patent applications, at least 36 foreign patents, and at least 21 pending foreign applications that are directed toward ARP-1536, and formulations or uses thereof. As of December 31, 2017, within the foregoing patent portfolio, we owned at least 21 U.S. patents, at least 9 pending U.S. provisional or non-provisional patent applications, at least 171 foreign patents, and at least 75 pending foreign applications that are directed toward AKB-9778, and formulations, medicinal chemistry variants, or uses thereof. As of December 31, 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 117 foreign patents, and at least 22 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, or ANDA 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 December 31, 2017, we had 25 full-time or part-time employees, including 13 employees with doctorate level degrees. Of these employees, 17 employees are engaged in research and development activities and 8 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.

Item 1A. Risk Factors.

The following risk factors and other information included in this Annual Report on Form 10-K should be carefully considered. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we presently deem less significant may also impair our business operations. Please see page 2 of this Annual Report on Form 10-K for a discussion of some of the forward-looking statements that are qualified by these risk factors. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

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 $21.4 million and $17.0 million for the years ended December 31, 2017 and 2016, respectively. As of December 31, 2017, we had an accumulated deficit of $108.6 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. 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, and we initiated a Phase 2b clinical trial in June 2017. Our product candidate AKB-4924 in our HIF-1-a stabilization program recently completed a Phase 1a trial and we expect to initiate a multiple ascending dose study in the second quarter of 2018. 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 or any of our other product candidates, our future revenues will depend upon the size of any markets in which AKB-9778 or any of our other product candidates 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 operating losses for the foreseeable future. We anticipate that our expenses will likely 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 December 31, 2017, our cash and cash equivalents were $20.3 million. We believe that we will continue to expend substantial resources for the foreseeable future developing AKB-9778 for diabetic retinopathy and any other indications that we may pursue, such as primary open angle glaucoma. Additionally, we expect to expend substantial resources to further develop AKB-4924, particularly as we prepare to initiate our planned multiple ascending dose study in the second quarter of 2018, as well as ARP-1536, for which we are evaluating development options. We may also expend substantial resources to develop any other product candidates that we may develop or acquire. 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 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.

Our auditors' report on our December 31, 2017 financial statements included an explanatory paragraph regarding there being substantial doubt about our ability to continue as a going concern.

We have a history of losses since inception and expect to continue to incur operating and net losses for the foreseeable future as we continue our research and development efforts and establish the necessary administrative functions to support our growing operations and being a public company, and such losses may increase in the future. Therefore, there is substantial doubt about our ability to continue operations in the future as a going concern, as highlighted by our auditors with respect to the financial statements for the year ended December 31, 2017. Although our financial statements raise substantial doubt about our ability to continue as a going concern, they do not reflect any adjustments that might result if we are unable to continue our business. If we cannot continue as a viable entity, our stockholders may lose some or all of their investment in our company.

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, 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. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. Only a small fraction of biopharmaceutical development programs ultimately results 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 our lead product candidate, AKB-9778, which is currently 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 rely on our lead product candidate, AKB-9778, which is currently in Phase 2 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, and which we plan to initiate a multiple ascending dose study in the second quarter of 2018. In addition, we are currently evaluating development options for ARP-1536. 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 substantially 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 intend to develop AKB-4924 and plan to initiate a multiple ascending dose study in the second quarter of 2018. With respect to ARP-1536, we are evaluating its development options. 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 or other product candidates. 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 Act 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;
- 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 statements.

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.

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 under 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.

On December 22, 2017, The Tax Cuts and Jobs Act (the "2017 Tax Act") was enacted and could have a material impact on our current and future income tax provision and disclosures.

Our effective tax rates could be affected by numerous factors, such as intercompany transactions, entry into new businesses and geographies, changes to our existing businesses and operations, acquisitions and investments and how they are financed, potential changes in our stock price, changes in our deferred tax assets and liabilities and their valuation, and changes in the relevant tax, accounting, and other laws, regulations, administrative practices, principles, and interpretations. Finally, U.S. State governments may enact tax laws in response to the 2017 Tax Act that could result in further changes to taxation and materially affect our financial position and results of operations.

The 2017 Tax Act significantly changes how the U.S. taxes corporations. The 2017 Tax Act requires complex computations to be performed that were not previously required in U.S. tax law, significant judgments to be made in interpretation of the provisions of 2017 Tax Act and significant estimates in calculations, and the preparation and analysis of information not previously relevant or regularly produced. The U.S. Treasury Department, the IRS, and other standard-setting bodies could interpret or issue guidance on how provisions of the 2017 Tax Act will be applied or otherwise administered that is different from our interpretation. As we complete our analysis of the 2017 Tax Act, collect and prepare necessary data, and interpret any additional guidance, we may make adjustments to amounts that we have provisionally recorded in the period in which the adjustments are made.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our corporate headquarters are located in Cincinnati, Ohio. We currently lease approximately 7,560 square feet of office space in Cincinnati under a lease that expires on June 30, 2018. We believe that our existing facilities are

adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms for our future growth.

Item 3. Legal Proceedings.

As of the date of this Annual Report on Form 10-K, we are not currently involved in any material legal proceedings. However, from time to time, we could be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Regardless of the outcome, legal proceedings can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Shares of our common stock were approved for trading and began trading on August 8, 2017 on the OTC Markets – OTCQB Tier under the symbol "ARPO." The following table sets forth the high and low closing bid information for our common stock for each quarterly period in the most recent fiscal year, as reported by OTCQB, since our common stock commenced public trading:

	Common Stock	
	High	Low
Year Ended December 31, 2017:		
Third Quarter	$ 6.75	$ 5.90
Fourth Quarter	$ 6.60	$ 4.00

Stockholders

As of February March 15, 2018, there were 266 stockholders of record of our common stock.

Dividends

We have never declared nor paid any cash dividends to stockholders. We do not intend to pay cash dividends on our common stock for the foreseeable future, and currently intend to retain any future earnings to fund our operations and the development and growth of our business. The declaration of any future cash dividends, if any, would be at the discretion of our Board of Directors (subject to limitations imposed under applicable Delaware law) and would depend on our earnings, if any, our capital requirements and financial position, our general economic conditions and other pertinent conditions.

Unregistered Sales of Securities

None

Unregistered Purchases of Equity Securities

None.

Item 6. Selected Financial Data.

Not applicable.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion of the financial condition and results of operations of Aerpio Pharmaceuticals, Inc. should be read in conjunction with the financial statements and the notes to those statements included in this Annual Report on Form 10-K for the period ended December 31, 2017. Some of the information contained in this discussion and analysis including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risk, uncertainties and assumptions. You should read the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

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 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 stop, slow down or 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. We expect to report top line results in the second quarter of 2019. 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 or more in DR Severity Score, or DRSS in the study 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.

In addition to DR and POAG, 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.

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 December 31, 2017, we had an accumulated deficit of $108.6 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 2017, we raised a total of $0.3 million through the issuance of secured convertible notes. In 2016, we raised a total of $12.5 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 operating losses for the foreseeable future. We expect our expenses will likely 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 accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern and do not include adjustments that might result from the outcome of this uncertainty. This basis of accounting contemplates the recovery of the Company's assets and the satisfaction of liabilities in the normal course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or amounts of liabilities that might be necessary should the Company be unable to continue as a going concern. The Company's inability to obtain required funding in the near future could have a material adverse effect on its operations and strategic development plan for future growth. If the Company cannot successfully raise additional capital and implement its strategic development plan, its liquidity, financial condition and business prospects will be materially and adversely affected, and the Company may have to cease operations. Based on the Company's current cash reserves of $20.3 million and current financial condition as of the date of the Annual Report on Form 10-K, there is substantial doubt about the Company's ability to continue as a going concern.

Basis of Presentation

The consolidated financial statements of the Company for the years ended December 31, 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 consolidated financial statements for the period ended December 31, 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 consolidated balance sheets and the consolidated statements of operation and comprehensive loss presented herein. The following discussion and analysis are based on the Company's consolidated financial statements contained in this Form 10-K, which we have prepared in accordance with United States generally accepted accounting principles. You should read the discussion and analysis together with such 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 Consolidated 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. General and administrative expenses have increased following 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 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 Consolidated Operations

Comparison of Years Ended December 31, 2017 and 2016

The following tables set forth our results of operations:

	Years Ended December 31,		$	%
	2017	2016	Change	Change
Operating expenses:				
Research and development	**$ 12,147,132**	$ 11,367,590	$ 779,542	7%
General and administrative	**9,241,411**	5,265,995	3,975,416	75%
Total operating expenses	**21,388,543**	16,633,585	4,754,958	29%
Loss from operations	**(21,388,543)**	(16,633,585)	(4,754,958)	29%
Grant income	**93,719**	131,281	(37,562)	-29%
Interest expense, net	**(105,782)**	(482,204)	376,422	-78%
Other income, net	**—**	997	(997)	-100%
Total other expense, net	**(12,063)**	(349,926)	337,863	-97%
Net and comprehensive loss	**$ (21,400,606)**	$ (16,983,511)	$(4,417,095)	26%

Research and Development

Research and development expenses for the year ended December 31, 2017, increased approximately $0.8 million, or 7%, compared to the year ended December 31, 2016. This increase was the result of increased spending on our lead program AKB-9778, currently in Phase 2b development, partially offset by a decrease in spending on our pipeline programs AKB 4924 and ARP 1536.

The approximate $3.5 million increase in spending on our lead program, AKB-9778, for the year ended December 31, 2017, from the corresponding period in 2016 is primarily attributed to the cost of drug product and clinical trial cost 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.

The approximate $2.7 million decrease in spending on our pipeline programs, for the year ended December 31, 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 of the pipeline programs. During the twelve months ended December 31, 2016, healthy volunteers were enrolled in the AKB-4924 Phase 1a clinical trial and cell line development expenses were incurred on ARP-1536, which were completed prior to 2017.

General and Administrative

General and administrative expenses in the twelve months ended December 31, 2017, increased approximately $4.0 million, or 75%, compared to the year ended December 31, 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, net

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. Grant income decreased in year ended December 31, 2017 compared to year ended December 31, 2016 primarily due to the expiration of various contracts during 2017.

Interest expense, net

Interest income in the year ended December 31, 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 twelve-month period in 2016, was primarily related to the senior secured convertible notes issued in 2016, offset in part by a small amount of interest income earned on invested cash balances. We completed three note financings in 2016 totaling an aggregate principal amount of approximately $12.5 million and one note financing in the first quarter of 2017, totaling an aggregate principal amount of approximately $0.3 million. The financings were funded in four tranches, beginning in April 2016 for $4.5 million, in July 2016 for $4.5 million, in October 2016 for $3.5 million and 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.

Other Income

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

Liquidity and Capital Resources

Since inception, we have incurred significant net losses. For the years ended December 31, 2017 and 2016, we had net losses of approximately $21.4 million and $17.0 million, respectively. Cash used in operating activities was $18.9 million and $15.7 million for the years 2017 and 2016, respectively, and investing activities used another $.1 million in 2016. Cash provided by financing activities was $37.5 million and $12.3 million for the years 2017 and 2016, respectively. At December 31, 2017 and 2016, we had an accumulated deficit of $108.6 million and $86.2 million, respectively.

At December 31, 2017, we had cash and cash equivalents of approximately $20.3 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 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:

	Year Ended December 31,	
	2017	**2016**
Net cash used in operating activities	**$ (18,883,536)**	$ (15,718,144)
Net cash provided by (used in) investing activities	**41,104**	(113,297)
Net cash provided by financing activities	**37,496,847**	12,296,924
Net increase (decrease) in cash and cash equivalents	**$ 18,654,415**	$ (3,534,517)

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 twelve months ended December 31, 2017, operating activities used approximately $18.9 million in cash, primarily as a result of our net loss of $21.4 million, offset by approximately $1.0 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 $1.5 million from changes in working capital. For the twelve months ended December 31, 2016, operating activities used approximately $15.7 million in cash, primarily as a result of our net loss of $17.0 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 and approximately $0.5 million from changes in working capital.

Investing Activities

Net cash provided by investing activities for the twelve months ended December 31, 2017 was due the sale of short-term investments, partially offset by capital expenditures to support our operations. Cash used in investing activities during the twelve months ended December 31, 2016 was due to the acquisition of approximately $0.1 million of laboratory equipment to support internal drug development capabilities.

Financing Activities

During the twelve months ended December 31, 2017, we received net proceeds of $37.2 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 twelve months ended December 31, 2016, we received $12.3 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 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.

For further information on the secured convertible notes see Note 6 to our consolidated financial statements.

Contractual Obligations and Commitments

The Company is a party to a lease covering 7,580 square feet of space in Cincinnati, Ohio that expires in June 2018. In November 2017, the Company renewed a lease covering 687 square feet of space in Dexter, MI that expires October 2019. Total rent expense for all operating leases was $208,478 and $214,595 for the years ended December 31, 2017 and 2016, respectively. The Cincinnati, Ohio space lease agreement contains free rent, escalating rent payments and reimbursement for tenant improvements that amounted to $46,390 in the year ended December 31, 2016. No such lease incentives were recognized in 2017. Rent expense for the Cincinnati, Ohio space 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 December 31, 2017, the Company had total deferred rent of $42,660 for the Cincinnati, Ohio space, which is included in accrued expenses in the accompanying consolidated balance sheet. As of December 31, 2017, non-cancelable future minimum lease payments under the existing operating leases were $76,650. We are contractually obligated to pay $65,890 of this in 2018 and the remainder, $10,760, in 2019.

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.

Off-Balance Sheet Arrangements

As of December 31, 2017 and 2016, we did not have any off-balance sheet arrangements as defined by applicable SEC regulations.

US Tax Reform

On December 22, 2017, The Tax Cuts and Jobs Act (the “2017 Tax Act”) was enacted, which is generally effective January 1, 2018. The Act includes a number of provisions, including lowering the U.S. corporate federal income tax rate from a maximum of 35% to 21% and changing or limiting certain tax deductions. In addition, the 2017 Tax Act alters the landscape of taxation and provides immediate deductions for certain new investments, among other provisions.

The significant impact as a result of adopting the 2017 Tax Act, was increased deferred tax expense due to the remeasurement of net deferred tax assets at the lower enacted U.S. federal corporate tax rate, which resulted in a net $11.3 million increase in deferred income tax expense, and had a corresponding $11.3 million offset to the valuation allowance.

The Company expects its effective income tax rate to remain at 0% for the foreseeable future as a result of the full recognition of a valuation allowance. Such estimates are based on management's current assumptions with respect to, among other things, the Company's earnings, state income tax levels and tax deductions.

The estimated impacts of the 2017 Tax Act recorded during 2017 as well as the forward-looking estimates are provisional in nature, and the Company will continue to assess the impact of the Act and provide additional information and record adjustments through the income tax provision in the relevant period as amounts are known and reasonably estimable during the measurement period. Accordingly, the impact of the 2017 Tax Act may differ from the Company's provisional estimates due to and among other factors, information currently not available, changes in interpretations and the issuance of additional guidance, as well as changes in assumptions the Company /has currently made, including actions the Company may take in future periods as a result of the 2017 Tax Act.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of financial position and results of consolidated operations are based on consolidated financial statements prepared in accordance with U.S. generally accepted accounting principles or GAAP. The preparation of these 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 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 consolidated financial statements.

Prepaid and Accrued Research and Development Expenses

As part of the process of preparing our 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 consolidated balance sheet date in our consolidated 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 consolidated 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 years ended December 31, 2017 and 2016, stock-based compensation expense was approximately $0.6 million and $0.5 million, respectively. As of December 31, 2017, we had $3.7 million of total unrecognized stock-based compensation costs for stock options, which we expect to recognize over a weighted-average period of 3.19 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 and prior to the merger, 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
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, at September 30, 2017, we used $6.00 per share and at December 31, 2017, we used $4.75 the closing share price on the OTCQB marketplace respectively on those dates. There were 1,014,014 and 50,228 stock option awards granted or issued in the years ended December 31, 2017 and 2016, respectively.

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 of 1933 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.

Recent Accounting Pronouncements

See Note 2 to the consolidated financial statements for a discussion of recent accounting pronouncements.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Interest Rate Risk

The Company’s cash and cash equivalents balance as of December 31, 2017 consisted primarily of cash held in an operating account that earns nominal interest income. Therefore, there was minimal or no interest rate risk.

Item 8. Consolidated Financial Statements and Supplementary Data.

Beginning on page 74 are the consolidated financial statements with applicable notes and the related Report of Independent Registered Public Accounting Firm.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Aerpio Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Aerpio Pharmaceuticals, Inc. (the Company) as of December 31, 2017 and 2016, and the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has recurring losses and negative cash flows from operations, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of these events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2011

Cincinnati, Ohio

March 15, 2018

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

AERPIO PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	Year Ended December 31,	
	2017	**2016**
Assets		
Current assets:		
Cash and cash equivalents	$ 20,264,109	$ 1,609,694
Short-term investments	—	50,000
Accounts receivable	—	4,157
Prepaid research and development contracts	313,140	353,434
Other current assets	322,221	209,038
Total current assets	20,899,470	2,226,323
Furniture and equipment, net	107,223	149,595
Deposits	20,960	20,960
Total assets	$ 21,027,653	$ 2,396,878
Liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable and accrued expenses	$ 3,592,164	$ 2,470,970
Convertible notes	—	12,386,647
Total current liabilities	3,592,164	14,857,617
Commitments and contingencies Note 13		
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 December 31, 2017 and 2016, respectively.	2,707	124
Additional paid-in capital	125,995,438	—
Accumulated deficit	(108,562,656)	(86,218,753)
Total stockholders' equity (deficit)	17,435,489	(86,218,629)
Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)	$ 21,027,653	$ 2,396,878

The accompanying notes are an integral part of these consolidated financial statements.

AERPIO PHARMACEUTICALS, INC.

Consolidated Statements of Operations and Comprehensive Loss

	Year Ended December 31,	
	2017	2016
Operating expenses:		
Research and development	$ 12,147,132	$ 11,367,590
General and administrative	9,241,411	5,265,995
Total operating expenses	21,388,543	16,633,585
Loss from operations	(21,388,543)	(16,633,585)
Grant income	93,719	131,281
Interest expense, net	(105,782)	(482,204)
Other income, net	—	997
Total other expense	(12,063)	(349,926)
Net and comprehensive loss	$ (21,400,606)	$ (16,983,511)
Reconciliation of net loss attributable to common stockholders:		
Net and comprehensive loss	$ (21,400,606)	$ (16,983,511)
Extinguishment of preferred stock	—	224,224
Adjustment of redeemable convertible preferred stock to redemption value	(943,297)	(4,152,801)
Net loss attributable to common stockholders	$ (22,343,903)	$ (20,912,088)
Net loss per share attributable to common stockholders, basic and diluted	$ (1.03)	$ (24.52)
Weighted average number of common shares used in computing net loss per share attributable to common stockholders, basic and diluted	21,673,349	852,665

The accompanying notes are an integral part of these consolidated financial statements.

AERPIO PHARMACEUTICALS, INC.

Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

	Redeemable Convertible Preferred Stock		Stockholders' Equity (Deficit)				
			Common Stock		Additional Paid-In	Accumulated	
	Shares	Total	Shares	Par Value	Capital	Deficit	Total
Balance at December 31, 2015	14,183,535	$ 70,487,415	1,157,251	$ 115	—	$ (66,554,870)	$ (66,554,755)
Adjustment of redeemable convertible preferred stock to redemption value	—	4,152,801	—	—	(1,273,631)	(2,879,170)	$ (4,152,801)
Conversion of preferred stock	(129,213)	(658,102)	61,803	6	658,096	—	$ 658,102
Extinguishment of preferred stock	(39,306)	(224,224)	—	—	25,426	198,798	$ 224,224
Conversion of convertible notes			—	—	82,818	—	$ 82,818
Issuance of common stock upon exercise of stock options	—	—	21,871	3	18,965	—	$ 18,968
Share-based compensation expense	—	—	—	—	488,326	—	$ 488,326
Net and comprehensive loss	—	—	—	—	—	(16,983,511)	$ (16,983,511)
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	—	—	—	—	649,409	—	649,409
Net and comprehensive loss	—	—	—	—	—	(21,400,606)	(21,400,606)
Balance at December 31, 2017	—	$ —	27,070,038	$ 2,707	$ 125,995,438	$ (108,562,656)	$ 17,435,489

The accompanying notes are an integral part of these consolidated financial statements.

AERPIO PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

	Year Ended December 31,	
	2017	**2016**
Operating activities:		
Net and comprehensive loss	$ (21,400,606)	$ (16,983,511)
Adjustments to reconcile net and comprehensive loss to net cash used in operating activities:		
Depreciation	51,268	69,673
Stock-based compensation	649,409	488,326
Amortization of debt issuance costs	75,561	188,686
Interest expense related to convertible note conversion	204,929	2,823
Changes in operating assets and liabilities:		
Accounts receivable	4,157	114,359
Prepaid expenses and current other assets	(72,889)	90,404
Accounts payable and other current liabilities	1,604,636	311,096
Net cash used in operating activities	(18,883,535)	(15,718,144)
Investing activities:		
Purchase of furniture and equipment	(8,896)	(113,297)
Proceeds from maturities of short-term investments	50,000	—
Net cash provided by (used in) investing activities	41,104	(113,297)
Financing activities:		
Proceeds from exercise of stock options	36,100	18,968
Proceeds from issuances of convertible notes	297,354	12,542,203
Cash paid for debt issuance costs	—	(264,247)
Proceeds from sale of common stock	40,247,777	—
Cash paid in connection with the sale of common stock	(3,084,385)	—
Net cash provided by financing activities	37,496,846	12,296,924
Net increase (decrease) in cash and cash equivalents	18,654,415	(3,534,517)
Cash and cash equivalents at beginning of year	1,609,694	5,144,211
Cash and cash equivalents, twelve months ended	$ 20,264,109	$ 1,609,694
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	—
Adjustment of redeemable convertible preferred stock to redemption value	943,297	4,152,801
Extinguishment of redeemable convertible preferred stock	—	(224,224)

The accompanying notes are an integral part of these consolidated financial statements.

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 has continued 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 were from Aerpio. In accordance with "reverse merger" or "reverse acquisition" accounting treatment, the consolidated financial statements for the period ended December 31, 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 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.

Going Concern Considerations

The Company incurred losses from operations and had a negative cash flows from operating activities for the years ended December 31, 2017 and 2016 and since inception. The Company's current operating plan indicates that it will continue to incur losses from operations and generate negative cash flows from operating activities given ongoing expenditures related to the completion of its ongoing clinical trials and the Company's lack of revenue generating activities. These events and conditions raise substantial doubt about the Company's ability to continue as a going concern.

The Company will need to raise additional funds in order to further advance its clinical research programs, commence additional clinical trials, and operate its business, and meet its obligations as they come due. The Company is pursuing financing alternatives, which include permanent equity financing, business development arrangements, licensing arrangements and business combination transactions. However, financing may not be available to the Company in the necessary time frame, in amounts that the Company requires, on terms that are acceptable to the Company, or at all. If the Company raises additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish valuable rights to its potential products or proprietary technologies, or grant licenses on terms that are not favorable to the Company. If the Company is unable to raise the necessary funds when needed or reduce spending on currently planned activities, it may not be able to continue the development of its product candidates or the Company could be required to delay, scale back, or eliminate some or all of its development programs and other operations and will materially harm its business, financial position and results of operations. Based on the company's current plans, it is anticipated that the existing cash and cash equivalents will allow the Company to conduct planned operations into the fourth quarter of 2018.

The accompanying consolidated financial statements have been prepared assuming that the company will continue as a going concern and do not include adjustments that might result from the outcome of this uncertainty. This basis of accounting contemplates the recovery of the company's assets and the satisfaction of liabilities in the normal course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or amounts of liabilities that might be necessary should the Company be unable to continue as a going concern. The company's inability to obtain required funding in the near future could have a material adverse effect on its operations and strategic development plan for future growth. If the company cannot successfully raise additional capital and implement its strategic development plan, its liquidity, financial condition and business prospects will be materially and adversely affected, and the Company may have to cease operations. Based on the Company's current cash reserves of $20.3 million and current financial condition as of the date of the Annual Report on Form 10-K, there is substantial doubt about the Company's ability to continue as a going concern.

2. Summary of Significant Accounting Policies

Basis of Presentation

The 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 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 consolidated financial statements are stated in U.S. Dollars.

The Company's consolidated financial statements are prepared in accordance with U.S. generally accepted accounting principles (U.S. GAAP) and 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 United States of America.

Use of Estimates

The preparation of 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 consolidated financial statements and the reported amounts of 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 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 stock-based awards.

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 included estimates and assumptions that required the Company's judgment. These estimates and assumptions included 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.

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 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 ASC 740*, 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 consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the consolidated 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 December 31, 2017, and 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 the year ended December 31, 2016, 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*. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock, to be recognized in the 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 ASC 820*, 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 years ended December 31, 2017 or 2016. The assets of the Company measured at fair value on a recurring basis as of December 31, 2017 and December 31, 2016 are summarized below:

	Fair Value Measurements Using			
	Level 1	Level 2	Level 3	Total
December 31, 2017				
Assets:				
Cash and cash equivalents	$ 20,264,109	$ —	$ —	$ 20,264,109
Total assets	$ 20,264,109	$ —	$ —	$ 20,264,109
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 December 31, 2017 and 2016, all the Company's cash and cash equivalents were 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 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 ASU 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 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)." This ASU addresses eight specific cash flow issues and applies to all entities that are required to present a statement of cash flows under FASB ASC Topic 230, *Statement of Cash Flows*. The amendments in this ASU are effective 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 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 consolidated statements of operations and comprehensive loss:

		Year Ended December 31,	
Activity	Consolidated Financial Statement Caption	2017	2016
Akebia related employee costs	Research and development operating expenses	$ —	$ 31,246
Facility-related reimbursement	Other income, net	—	1,994

4. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses are as follows:

	December 31, 2017	December 31, 2016
Accounts payable	**$ 1,276,537**	$ 1,135,608
Professional fees	**277,217**	200,468
Accrued bonus	**833,650**	—
Accrued interest	**—**	483,442
Accrued vacation	**69,549**	52,835
Accrued project costs	**1,069,852**	541,158
Other	**65,359**	57,459
Total accounts payable and accrued expenses	**$ 3,592,164**	$ 2,470,970

5. Furniture and Equipment

Furniture and equipment and accumulated depreciation balances are as follows:

	December 31, 2017	December 31, 2016
Furniture	**$ 156,928**	$ 156,928
Computers	**109,204**	111,446
Equipment	**141,067**	141,067
Leasehold improvements	**35,869**	35,869
Total furniture and equipment	**443,068**	445,310
Accumulated depreciation	**(335,845)**	(295,715)
Furniture and equipment, net	**$ 107,223**	$ 149,595

6. 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 December 31, 2017 and 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 financing (the "Additional Convertible Notes" or the "Additional Convertible Note Financing") 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.

7. Common Stock

As of December 31, 2017 and 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"). As of December 31, 2017, the Lock-Up Agreements have expired.

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 December 31, 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 year ended December 31, 2017.

Warrants to Purchase Common Stock

At December 31, 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 warrants, 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 common stock splits, combinations, reorganizations, or issue shares as part of a common 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 common stock.

8. Preferred Stock

At December 31, 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 December 31, 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 are payable, if permitted by law, in accordance with redeemable convertible preferred stock terms or when and if declared by Aerpio Board of Directors.

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.

9. Stock-Based Compensation

On November 17, 2011, the Company established the Aerpio Therapeutics, Inc. 2011 Equity Incentive Plan (the Plan). The Plan allows for the grant of either incentive stock options or non-qualified stock options to purchase Common Stock, stock bonuses, or restricted stock awards for management and certain persons performing services for the Company. As of December 31, 2016, a total of 5,860,874 shares of Common Stock were authorized for issuance in accordance with the provisions of the Plan.

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.

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. Five option awards were granted for 1,014,018 shares in the twelve months ended December 31, 2017 and one option award was granted for 50,228 shares in the twelve months ended December 31, 2016. In 2017, two option awards for 733,570 shares were inducement grants related to hiring the CEO and CFO and three option awards for 280,448 shares were issued under the 2017 Equity Plan. Three option awards for 280,448 shares were granted under the 2017 Plan as of December 31, 2017. At December 31, 2017, 3,391,960 shares are reserved for issuance under the 2017 Plan.

The following table summarizes the stock option activity during the year ended December 31, 2017:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding, January 1, 2016	907,485	$ 1.66		$ 135,711
Granted	50,228	$ 1.80		
Exercised	(21,870)	0.87		
Expired/cancelled	(8,251)	1.24		
Outstanding, December 31, 2016	927,592	$ 1.70	7.48	$ 1,030,217
Expected to vest, December 31, 2016	312,547	$ 1.82	8.60	$ 308,767
Options exercisable, December 31, 2016	615,045	$ 1.63	6.92	$ 721,451
Outstanding, January 1, 2017	927,592	$ 1.70	7.48	$ 1,030,217
Granted	1,014,018	$ 5.50		
Exercised	(25,729)	1.40		
Expired/cancelled	(2,901)	2.11		
Outstanding, December 31, 2017	1,912,980	$ 3.72	8.24	$ 2,738,704
Expected to vest, December 31, 2017	1,161,495	$ 5.02	9.65	$ 441,553
Options exercisable, December 31, 2017	751,485	$ 1.69	6.07	$ 2,297,151

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. The aggregate intrinsic value of the options at December 31, 2016 was $1,030,217.

The weighted average grant date fair value of stock options granted during the year ended 2017 was $3.39. Stock options exercised during 2017 and 2016 had an intrinsic value of $92,544 and $20,335, respectively.
Compensation expense for stock options was $327,649 and $180,399 for the year ended December 31, 2017 and 2016, respectively. As of December 31, 2017, there was $3,517,806 of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted average period of 3.31 years.

The Company uses the Black-Scholes option pricing model to determine the estimated fair value for stock-based awards. There were 1,014,018 and 50,228 options granted in the years ended December 31 ,2017 and 2016, respectively. 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. As there has been significant public market activity of the Company's Common Stock, the Company has determined the volatility assumption for options granted based on data from a peer group of companies that issued options with substantially similar terms. The expected volatility of options granted has been determined using the average of the historical volatility measures of this peer group of companies for a period equal to the expected life of the option. The risk-free interest rate is based on the rate applicable to U.S. Treasury zero-coupon issues, with remaining maturities commensurate with the expected term of the options granted in effect on the date of grant. The Company has not paid, and does not anticipate paying, cash dividends on shares of Common Stock; therefore, the expected dividend yield is assumed to be zero in the option valuation model. Accordingly, the weighted-average fair value of the options granted during the years ended December 31, 2017 and 2016 was $3.39 and $1.22 respectively. The calculation was based on the following assumptions.

	Year Ended December 31,	
	2017	**2016**
Expected term (years)	**5.94**	6.00
Risk-free interest rate	**2.19%**	1.39%
Expected volatility	**67.57%**	61.00%
Expected dividend yield	—	—

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 twelve year ended December 31, 2017 is as follows:

	Shares	**Weighted Average Grant Date Fair Value**
Nonvested, January 1, 2016	444,199	$ 1.69
Granted	—	—
Vested	(203,103)	1.54
Forfeited	—	—
Nonvested, December 31, 2016	241,096	$ 1.91
Nonvested, January 1, 2017	241,096	$ 1.91
Granted	—	—
Vested	(144,274)	1.91
Forfeited	(5,246)	2.20
Nonvested, December 31, 2017	91,576	$ 2.12

The Company recognized compensation expense for restricted stock of $321,760 and 307,927 for the years ended December 31, 2017 and 2016 respectively. As of December 31, 2017, there was $169,933 of unrecognized compensation cost related to these restricted stock grants, which is expected to be recognized over a weighted average period of .69 years.

Compensation Expense Summary

The Company has recognized the following compensation cost related to employee and non-employee stock-based compensation activity:

	Year Ended December 31,	
	2017	2016
Research and development	**$ 393,347**	$ 317,644
General and administrative	**256,062**	170,682
Total	**$ 649,409**	$ 488,326

10. Income Taxes

The 2017 Tax Act was signed into law on December 22, 2017. The 2017 Tax Act significantly revises the U.S. corporate income tax by, among other things, lowering the statutory corporate tax rate from 35% to 21% in 2018, eliminating certain deductions, imposing a mandatory one-time transition tax, or deemed repatriation tax, on accumulated earnings of foreign subsidiaries as of 2017 that were previously tax deferred, introducing new tax regimes, and changing how foreign earnings are subject to U.S. tax. While the effective date of the new corporate tax rates for the Company is January 1, 2018, the Company is required to calculate the effects of changes in tax rates and laws on deferred tax balances in 2017, the period in which the legislation was enacted. The impact of the 2017 Tax Act on the 2017 income tax provision was primarily related to the newly enacted lower statutory federal corporate tax rate. The Company is not impacted by the one-time transition tax.

The Company has not completed its determination of the accounting implications of the 2017 Tax Act on its tax accruals. However, the Company has reasonably evaluated an income tax expense as a provisional estimate of the 2017 Tax Act, fully offset by a corresponding valuation allowance. The significant component of this expense primarily relates to the remeasurement of net deferred tax assets at the lower enacted statutory federal corporate tax rate. As the Company completes its analysis of the 2017 Tax Act, collects and prepares necessary data, and interprets any additional guidance issued by the U.S. Treasury Department, the IRS, and other standard-setting bodies, the Company may make adjustments to the provisional amounts. Those adjustments may materially impact the Company's provision for income taxes in the period in which the adjustments are made.

The Company did not record a current or deferred income tax expense or benefit for the years ended December 31, 2017 and 2016, due to the Company's net losses and increases in its deferred tax asset valuation allowance. The components of loss before income taxes and a reconciliation of the statutory federal income tax with the provision for income taxes are as follows:

	Year Ended December 31,	
	2017	2016
Federal tax at statutory rate	**(34.00%)**	(34.00%)
State and local tax at statutory rates, net of federal income tax	**(0.83)**	(0.83)
Research and development credits	**(1.72)**	(3.77)
Other	**1.42**	1.32
Change in valuation allowance	**(17.64)**	37.28
Remeasurement of U.S. net deferred tax assets from 35% to 21%	**52.77**	0.00
Effective tax rate	**0.00%**	0.00%

The Company's income tax provision was computed based on the federal statutory rate and the average state statutory rates, net of the related federal benefit.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of the assets and liabilities for financial reporting purposes and the amounts used for income and for tax carryforwards, recorded at the enacted federal statutory income tax rate. Significant components of the Company's deferred tax assets and liabilities are as follows:

	December 31,	
	2017	**2016**
Deferred tax assets:		
Net operating loss carryforwards	**$ 18,819,077**	$ 23,146,178
Accrued expenses	**204,599**	18,400
Stock-based compensation	**96,578**	96,570
Research and development credits	**3,038,863**	2,670,688
Other	**13,953**	20,784
Total deferred tax assets	**$ 22,173,070**	$ 25,952,620
Deferred tax liabilities:		
Fixed assets	**3,606**	8,434
Total deferred tax liabilities	**3,606**	8,434
Net deferred tax assets before valuation allowance	**22,169,464**	25,944,186
Less valuation allowance	**(22,169,464)**	(25,944,186)
Net deferred tax asset	**$ —**	$ —

When realization of the deferred tax asset is more likely than not to occur, the benefit related to the deductible temporary differences attributable to operation is recognized as a reduction of income tax expense. Valuation allowances are provided against deferred tax assets when, based on all available evidence, it is considered more likely than not that some portion or all of the recorded deferred tax assets will not be realized in future periods. The Company cannot be certain that future taxable income will be sufficient to realize its deferred tax assets, and accordingly, a full valuation allowance has been provided on its net deferred tax assets. The valuation allowance decreased $3,774,722 in 2017 primarily as a result of the changes in the 2017 Tax Act offset by an increase with allowance on the NOL carryforward and increased $6,334,258 in 2016 as a result of an increase in the net operating loss (NOL) due to research and development credits carryforwards. The Company continues to monitor the need for a valuation allowance based on the profitability of its future operations.

At December 31, 2017, the Company has approximately $86,346,064 of federal NOL carryforwards that have a 20-year carryforward period expiring at various dates through 2038. Additionally, the Company also has approximately $69,509,257 of state NOL carryforwards that expire from 2018 through 2038. Finally, at December 31, 2017, the Company had approximately $3,038,863 of federal research and development credit carryforwards that expire at various dates through 2038.

Under the provisions of the Internal Revenue Code, NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. NOL and tax credit carryforwards may be subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders by more than 50% over a three-year period, as defined in Sections 382 and 383 of the Internal Revenue Code and similar state provisions. The amount of the annual limitation is determined based on the value of the Company immediately before the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not completed a study to assess whether a change of control has occurred or whether there have been multiple changes of control since the date of the Company's formation due to the significant complexity and cost associated with such study and that there could be additional changes in control in the future. As a result, the Company is unable to estimate the effect of these limitations, if any, on the Company's ability to utilize NOL and tax credit carryforwards in the future.

The Company has not yet conducted a study to document whether its research activities may qualify for the research and development tax credit. Such a study may result in an adjustment to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credit and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the research and development credit carryforwards and the valuation allowance.

As of December 31, 2017 and 2016, the Company had no accrued uncertain tax positions or associated interest or penalties and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive loss.

The Company files income tax returns in the U.S. federal jurisdiction and various state jurisdictions. All years remain open and are subject to examination by federal and state taxing authorities.

11. 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:

	Year Ended December 31,	
	2017	**2016**
Net and comprehensive loss	**$ (21,400,606)**	$ (16,983,511)
Extinguishment of preferred stock	**—**	224,224
Adjustment of redeemable convertible preferred stock to redemption value	**(943,297)**	(4,152,801)
Net loss attributable to common stockholders	**$ (22,343,903)**	$ (20,912,088)
Net loss per share attributable to common stockholders, basic and diluted	**$ (1.03)**	$ (24.52)
Weighted average common shares used in computing net loss per share attributable to common stockholders, basic and diluted	**21,673,349**	852,665

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:

	December 31,	
	2017	**2016**
Convertible preferred stock (if converted)	**—**	14,015,016
Notes and accrued interest (if converted)	**—**	2,641,602
Options to purchase common stock	**1,912,980**	927,592
Warrants to purchase common stock	**317,562**	—

12. Quarterly Results (unaudited)

The following is a summary of our unaudited quarterly results for the years ended December 31, 2017 and 2016.

	Quarter Ended				
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017	Total 2017
			(unaudited)		
Total operating expenses	$ 4,759,585	$ 5,583,862	$ 4,756,238	$ 6,288,858	$ 21,388,543
Loss from operations	(4,759,585)	(5,583,862)	(4,756,238)	(6,288,858)	(21,388,543)
Total other (expense) income, net	(236,118)	63,555	106,671	53,829	$ (12,063)
Net loss and comprehensive loss	$ (4,995,703)	$ (5,520,307)	$ (4,649,567)	$ (6,235,029)	$ (21,400,606)
Reconciliation to net loss attributable to common stockholders:					
Net loss and comprehensive loss	$ (4,995,703)	$ (5,520,307)	$ (4,649,567)	$ (6,235,029)	$ (21,400,606)
Adjustment of redeemable convertible preferred stock to redemption value	(943,297)	—	—	—	$ (943,297)
Net loss attributable to common stockholders	(5,939,000)	(5,520,307)	(4,649,567)	(6,235,029)	(22,343,903)
Weighted average number of common shares used in computing net loss per share attributable to common stockholders, basic and diluted	5,605,151	26,895,164	26,926,673	26,965,293	21,673,349
Net loss per share attributable to common stockholders, basic and diluted	$ (1.06)	$ (0.21)	$ (0.17)	$ (0.23)	$ (1.03)

	Quarter Ended				
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016	Total 2016
			(unaudited)		
Total operating expenses	$ 4,205,443	$ 4,377,433	$ 4,745,315	$ 3,305,394	$ 16,633,585
Loss from operations	(4,205,443)	(4,377,433)	(4,745,315)	(3,305,394)	(16,633,585)
Total other income (expense), net	10,745	(7,829)	(140,286)	(212,556)	(349,926)
Net loss and comprehensive loss	$ (4,194,698)	$ (4,385,262)	$ (4,885,601)	$ (3,517,950)	$ (16,983,511)
Reconciliation to net loss attributable to common stockholders:					
Net loss and comprehensive loss	$ (4,194,698)	$ (4,385,262)	$ (4,885,601)	$ (3,517,950)	$ (16,983,511)
Extinguishment of preferred stock	—	224,224	—	—	224,224
Adjustment of redeemable convertible preferred stock to redemption value	(1,015,371)	(1,028,121)	(1,054,657)	(1,054,652)	(4,152,801)
Net loss attributable to common stockholders	$ (5,210,069)	$ (5,189,159)	$ (5,940,258)	$ (4,572,602)	$ (20,912,088)
Weighted average number of common shares used in computing net loss per share attributable to common stockholders, basic and diluted	737,016	823,097	888,094	961,482	852,665
Net loss per share attributable to common stockholders, basic and diluted	$ (7.07)	$ (6.30)	$ (6.69)	$ (4.76)	$ (24.52)

The sum of the quarterly net loss per share attributable to common stockholders may not equal the annual amounts reported because per share amounts are computed independently for each quarter and for full year based on respective weighted-average common shares outstanding and other dilutive potential common stockholders.

13. 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. In November 2017, the Company renewed a lease covering 687 square feet of space in Dexter, MI that expires October 2019. Total rent expense for all operating leases was $208,478 and $214,595 for the years ended December 31, 2017 and 2016, respectively. The Cincinnati, Ohio space lease agreement contains free rent, escalating rent payments and reimbursement for tenant improvements that amounted to $46,390 in the year ended December 31, 2016. No such lease incentives were recognized in 2017. Rent expense for the Cincinnati, Ohio space 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 December 31, 2017, the Company had total deferred rent of $42,660 for the Cincinnati, Ohio space, which is included in accrued expenses in the accompanying consolidated balance sheet. As of December 31, 2017, non-cancelable future minimum lease payments under the existing operating leases were $76,650. As of December 31, 2017, future payments related to operating leases activities are as follows:

	2018	2019 and Thereafter	Total
Operating leases	$ 65,890	$ 10,760	$ 76,650

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.

14. Employee Retirement Plan

The Company created Aerpio's 401(k) plan in 2015. Before then, the Company's employees participated in Akebia's 401(k) plan (Akebia Plan) collectively, the Plans. In accordance with both Plans, all employees who have attained the age of 21 are eligible to participate in the Plan as of the first Entry Date, as defined, following the employment date. Each employee can contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary, and no contributions were made during 2017 or 2016.

15. Employee Bonus Plan

The Company maintains a bonus plan for certain employees of the Company based on the achievement of certain milestones. The amount of bonus accrued at December 31, 2017 was $833,650. No bonus was accrued or paid at December 31, 2016.

16. 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. No shares were purchased under the ESPP during 2017. 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.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

The Company maintains disclosure controls and procedures that are designed to provide reasonable assurance that information required to be disclosed in the Company's reports under the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including the Company's Chief Executive Officer ("CEO") and Chief Financial Officer ("CFO"), as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. Management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

In connection with the preparation of this Annual Report on Form 10-K, an evaluation is performed under the supervision and with the participation of the Company's management, including the CEO and CFO, of the effectiveness of the design and operation of the Company's disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act) as of December 31, 2017. Based on that evaluation, the CEO and CFO conclude whether the Company's disclosure controls and procedures are effective as of December 31, 2017, at the reasonable assurance level.

In connection with this Annual Report on Form 10-K for the year ended December 31, 2017, an evaluation was performed of the effectiveness of the design and operation of the Company's disclosure controls and procedures as of December 31, 2017. Based on that evaluation, the CEO and CFO concluded that the disclosure controls and procedures were effective as of December 31, 2017, at the reasonable assurance level.

Management's Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting for us. Internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) is a process to provide reasonable assurance regarding the reliability of our financial reporting for external purposes in accordance with U.S. generally accepted accounting principles. Internal control over financial reporting includes maintaining records that in reasonable detail accurately and fairly reflect our transactions; providing reasonable assurance that transactions are recorded as necessary for preparation of our consolidated financial statements; providing reasonable assurance that receipts and expenditures of company assets are made in accordance with management authorization; and providing reasonable assurance that unauthorized acquisition, use or disposition of company assets that could have a material effect on our consolidated financial statements would be prevented or detected on a timely basis. Because of its inherent limitations, internal control over financial reporting is not intended to provide absolute assurance that a misstatement of our consolidated financial statements would be prevented or detected.

Management conducted an evaluation of the effectiveness, as of December 31, 2017, of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013. Based on this evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2017.

Changes in Internal Controls over Financial Reporting

In connection with the preparation of the Company's financial statements for the year ended December 31, 2016, certain matters involving internal control over financial reporting rose to the level of a material weakness. The material weakness related to deficiencies within the Company's disclosure controls and procedures, including review and approval procedures with respect to financial information generated to prepare the financial statements in accordance with SEC financial reporting requirements. This material weakness included a general lack of segregation of duties as a result of the Company's size and overall lack of resources in the accounting department.

This material weakness in our disclosure controls and procedures continued to exist as of the first three quarters of 2017. In the fourth quarter of 2017, this material weakness was remediated as a result of the following actions taken during the year:

- A new full-time CFO was hired in 2017;
- We engaged with a third-party consultant with internal control expertise to help with our management internal control assessment;

/s/ Stephen Hoffman, M.D., Ph.D.
Stephen Hoffman
Chief Executive Officer

/s/ Michael Rogers
Michael Rogers
Chief Financial Officer

March 15, 2018

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The other information required by this item is omitted from this Annual Report on Form 10-K and is incorporated herein by reference from our definitive proxy statement relating to our 2018 Annual Meeting of Stockholders (the "Definitive Proxy Statement").

Code of 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. Our code of business conduct and ethics is available on our website, which is located at www.aerpio.com. We intend to disclose any amendments to the code, or any waivers of its requirements, on our website, or in a current report on Form 8-K as may be required by law.

Item 11. Executive Compensation.

The information required by this Item 11 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be contained in the Definitive Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statements.

(a) (1) Financial Statements.

The consolidated financial statements required by this item are submitted in a separate section beginning on page 74 of this report.

(a)(2) Exhibits.

Exhibit Index

Exhibit Number	Description
2.1	Agreement and Plan of Merger, dated March 7, 2017, by and among the Company, Acquisition Sub, a Delaware corporation and wholly-owned subsidiary of the Company, and Aerpio Therapeutics, Inc., a Delaware corporation (incorporated herein by reference to Exhibit 2.1 to the Company's 8-K filed with the Securities and Exchange Commission on March 13, 2017, File No. 000-53057).
3.1	Certificate of Merger relating to the merger of Acquisition Sub with and into Aerpio Therapeutics, Inc., filed with the Secretary of State of the State of Delaware on March 15, 2017 (incorporated herein by reference to Exhibit 3.1 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057).
3.2	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)
3.3	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	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)
10.1#	2011 Equity Incentive Plan and forms of award agreements thereunder, assumed in the Merger (incorporated herein by reference to Exhibit 10.1 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.1.2#	Amended and Restated 2017 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.1 to the Company's 8-K filed with the Securities and Exchange Commission on December 18, 2017, File No. 000-53057)
10.2#	2017 Stock Option and Incentive Plan and forms of award agreements thereunder (incorporated herein by reference to Exhibit 10.2 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.3#	2017 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.3 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.4#	Form of Indemnification Agreement (incorporated herein by reference to Exhibit 10.4 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.5	Registration Rights Agreement, dated March 15, 2017, by and among the Company and the persons listed on Exhibit A attached thereto (incorporated herein by reference to Exhibit 10.5 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.6	Subscription Agreement, dated March 15, 2017, by and between the Company and the investors party thereto (incorporated herein by reference to Exhibit 10.6 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)

10.7	Office Lease at 10300 Alliance Road, Cincinnati, OH dated as of September 29, 2009, by and between Akebia Therapeutics, Inc. and Duke Realty Ohio, as amended by the First Lease Amendment dated as of April 23, 2010 by and between Akebia Therapeutics, Inc. and Duke Realty Ohio, as amended by the Second Lease Amendment and Assignment and Assumption of Lease dated as of April 25, 2012 by and between DP Landings Building II, LLC, Akebia Therapeutics, Inc., and Aerpio, as amended by the Third Amendment to Office Lease dated as of February 27, 2015 by and between RT Landings Building II, LLC and Aerpio (incorporated herein by reference to Exhibit 10.7 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.8#	Employment Agreement, dated as of March 15, 2017, between the Company and Joseph H. Gardner (incorporated herein by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 filed with the Securities and Exchange Commission on April 14, 2017, File No. 333-217320)
10.9#	Employment Agreement, dated as of March 15, 2017, between the Company and Kevin G. Peters (incorporated herein by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1 filed with the Securities and Exchange Commission on April 14, 2017, File No. 333-217320)
10.10#	Employment Agreement, dated as of March 15, 2017, between the Company and Stephen Pakola (incorporated herein by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 filed with the Securities and Exchange Commission on April 14, 2017, File No. 333-217320)
10.11	Employment Agreement, entered into on October 8, 2017, by and between the Company and Stephen Hoffman (incorporated herein by reference to Exhibit 10.1 to the Company's 8-K filed with the Securities and Exchange Commission on October 10, 2017, File No. 000-53057)
10.12	First Amendment to Employment Agreement, dated October 8, 2017, by and between the Company and Joseph Gardner (incorporated herein by reference to Exhibit 10.1 to the Company's 8-K filed with the Securities and Exchange Commission on October 10, 2017, File No. 000-53057)
10.13	Employment Agreement, effective as of November 15, 2017, by and between the Company and Michael Rogers (incorporated herein by reference to Exhibit 10.1 to the Company's 8-K filed with the Securities and Exchange Commission on November 14, 2017, File No. 000-53057)
10.14	Registration Rights Agreement by and among the Company and certain former stockholders of Aerpio (incorporated herein by reference to Exhibit 10.9 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057).
10.15*	Senior Cash Incentive Bonus Plan of the Company
21.1	Subsidiaries of the Registrant (incorporated herein by reference to Exhibit 21.1 to the Company's 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057).
23.1*	Consent of Ernst & Young LLP
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document

101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.
\# Indicates a management contract or any compensatory plan, contract or arrangement.

Item 16. Form of 10-K Summary

We may voluntarily include a summary of information required by Form 10-K under this Item 16. We have elected not to include such summary information.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

AERPIO PHARMACEUTICALS, INC.

Date: March 15, 2018

By: */s/ Stephen Hoffman, M.D., Ph.D.*
Stephen Hoffman, M.D., Ph.D.
Chief Executive Officer and Principal Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates 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	March 15, 2018
/s/ Michael Rogers **Michael Rogers**	Chief Financial Officer and Principal Financial and Accounting Officer	March 15, 2018
/s/ Joseph Gardner, Ph.D **Joseph Gardner**	Director, President and Founder	March 15, 2018
/s/ Muneer A. Satter **Muneer A. Satter**	Director	March 15, 2018
/s/ Chau Khuong **Chau Khuong**	Director	March 15, 2018
/s/ Steven Prelack **Steven Prelack**	Director	March 15, 2018
/s/ Paul Weiss, Ph.D **Paul Weiss**	Director	March 15, 2018
/s/ Caley Castelein, M.D. **Caley Castelein**	Director	March 15, 2018
/s/ Anupam Dalal, M.D. **Anupam Dalal**	Director	March 15, 2018
/s/ Pravin Dugel, M.D. **Pravin Dugel**	Director	March 15, 2018

AERPIO PHARMACEUTICALS, INC.
SENIOR EXECUTIVE CASH INCENTIVE BONUS PLAN

Purpose

This Senior Executive Cash Incentive Bonus Plan (the "***Incentive Plan***") is intended to provide an incentive for superior work and to motivate eligible executives of Aerpio Pharmaceuticals, Inc. (the "***Company***") and its subsidiaries toward even higher achievement and business results, to tie their goals and interests to those of the Company and its stockholders and to enable the Company to attract and retain highly qualified executives. The Incentive Plan is for the benefit of Participants (as defined below).

Participants

From time to time, the Board of Directors of the Company (the "***Board***") may select certain key executives (the "***Participants***") to be eligible to receive bonuses hereunder. Participation in this Plan does not change the "at will" nature of a Participant's employment with the Company.

Administration

The Board shall have the sole discretion and authority to administer and interpret the Incentive Plan.

Bonus Determinations

Corporate Performance Goals. A Participant may receive a bonus payment under the Incentive Plan based upon the attainment of one or more performance objectives that are established by the Board and relate to financial and operational metrics with respect to the Company or any of its subsidiaries (the "***Corporate Performance Goals***"), including 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 the Company's 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 the Company's 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 (i) measured in absolute terms or compared to any incremental increase, (ii) measured in terms of growth, (iii) compared to another company or companies or to results of a peer group, (iv) measured against the market as a whole and/or as compared to applicable market indices and/or (v) measured on a pre-tax or post-tax basis (if applicable). Further, any Corporate Performance Goals may be used to measure the performance of the Company as a whole or a business unit or other segment of the Company, or one or more product lines or specific markets. The Corporate Performance Goals may differ from Participant to Participant.

Calculation of Corporate Performance Goals. At the beginning of each applicable performance period, the Board will determine whether any significant element(s) will be included in or excluded from the calculation of any Corporate Performance Goal with respect to any Participant. In all other respects, Corporate Performance Goals will be calculated in accordance with the Company's financial statements, generally accepted accounting principles, or under a methodology established by the Board at the beginning of the performance period and which is consistently applied with respect to a Corporate Performance Goal in the relevant performance period.

Target; Minimum; Maximum. Each Corporate Performance Goal shall have a "target" (100 percent attainment of the Corporate Performance Goal) and may also have a "minimum" hurdle and/or a "maximum" amount.

Bonus Requirements; Individual Goals. Except as otherwise set forth in this Section 4(d): (i) any bonuses paid to Participants under the Incentive Plan shall be based upon objectively determinable bonus formulas that tie such bonuses to one or more performance targets relating to the Corporate Performance Goals, (ii) bonus formulas for Participants shall be adopted in each performance period by the Board and communicated to each Participant at the beginning of each performance period and (iii) no bonuses shall be paid to Participants unless and until the Board makes a determination with respect to the attainment of the performance targets relating to the Corporate Performance Goals. Notwithstanding the foregoing, the Board may adjust bonuses payable under the Incentive Plan based on achievement of one or more individual performance objectives or pay bonuses (including, without limitation, discretionary bonuses) to Participants under the Incentive Plan based on individual performance goals and/or upon such other terms and conditions as the Board may in its discretion determine.

Individual Target, Minimum and Maximum Bonuses. The Board shall establish a target bonus opportunity for each Participant for each performance period. For each Participant, the Board shall have the authority to apportion the target award so that a portion of the target award shall be tied to attainment of Corporate Performance Goals and a portion of the target award shall be tied to attainment of individual performance objectives. The Board may also establish award payouts below or above a Participant's target bonus opportunity for attainment of Corporate Performance Goals at Minimum or Maximum amounts defined in Section 4(c) above.

Employment Requirement. Subject to any additional terms contained in a written agreement between the Participant and the Company, the payment of a bonus to a Participant with respect to a performance period shall be conditioned upon the Participant's employment by the Company on the bonus payment date. If a Participant was not employed for an entire performance period, the Board may pro rate the bonus based on the number of days employed during such period.

Timing of Payment

With respect to Corporate Performance Goals established and measured on a basis more frequently than annually (e.g., quarterly or semi-annually), the Corporate Performance Goals will be measured at the end of each performance period after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for such period are met, payments will be made as soon as practicable following the end of such period, but not later 74 days after the end of the fiscal year in which such performance period ends.

With respect to Corporate Performance Goals established and measured on an annual or multi-year basis, Corporate Performance Goals will be measured as of the end of each such performance period (e.g., the end of each fiscal year) after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for any such period are met, bonus payments will be made as soon as practicable, but not later than 74 days after the end of the relevant fiscal year.

For the avoidance of doubt, bonuses earned at any time in a fiscal year must be paid no later than 74 days after the last day of such fiscal year.

Amendment and Termination

The Company reserves the right to amend or terminate the Incentive Plan at any time in its sole discretion.

* * * * *

Adopted March 15, 2017.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-220057) pertaining to the Aerpio Therapeutics, Inc. 2011 Equity Incentive Plan, Aerpio Pharmaceuticals, Inc. 2017 Stock Option and Incentive Plan, and Aerpio Pharmaceuticals, Inc. 2017 Employee Stock Purchase Plan, and
(2) Registration Statement (Form S-3 No. 333-223113) of Aerpio Pharmaceuticals, Inc.,

of our report dated March 15, 2018, with respect to the consolidated financial statements of Aerpio Pharmaceuticals, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Cincinnati, Ohio
March 15, 2018

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Stephen Hoffman, certify that:

1. I have reviewed this annual report on Form 10-K of Aerpio Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2018

By: */s/ Stephen Hoffman, M.D., Ph.D.*
Stephen Hoffman, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael Rogers, certify that:

1. I have reviewed this annual report on Form 10-K of Aerpio Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313);

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

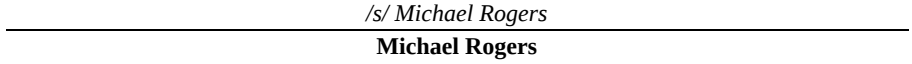
   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2018

By: *  *

Michael Rogers
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Aerpio Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ending December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 15, 2018

By: */s/ Stephen Hoffman, M.D., Ph.D.*

Stephen Hoffman, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Aerpio Pharmaceuticals, Inc. (the "Company") on Form 10-K for the period ending December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 15, 2018

By: */s/ Michael Rogers*

Michael Rogers
Chief Financial Officer
(Principal Financial Officer and Principal Accounting Officer)