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, 2020

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 001-38560

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:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, $0.0001 par value per share	ARPO	Nasdaq Capital 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 every Interactive Data File required to be submitted 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 such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a 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	☒	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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on June 30, 2020 was approximately $49,213,310.

The number of shares of registrant's common stock outstanding as of March 8, 2021 was 47,313,338.

DOCUMENTS INCORPORATED BY REFERENCE

Summary of the Material and Other Risks Associated with Our Business

Our business is subject to numerous risks and uncertainties that you should be aware of in evaluating our business, including those described in Part II, Item IA. "Risk Factors" in this Annual Report on Form 10-K. These risks include, but are not limited to, the following:

- We cannot assure you that our exploration of strategic alternatives will result in a transaction or that any such transaction would be successful, and the process of exploring strategic alternatives or its conclusion could adversely impact our business and our stock price.
- The current pandemic of COVID-19 and the future outbreak of other highly infectious or contagious diseases could seriously harm our research, development and potential future commercialization efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.
- We depend heavily on the success of our lead product candidate, razuprotafib. Even if we obtain favorable clinical results, we may not be able to obtain regulatory approval for, or successfully commercialize, razuprotafib.
- We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.
- Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from preclinical studies or earlier stage clinical trials are not necessarily predictive of the results of our future clinical trials of razuprotafib. If we cannot replicate the positive results from preclinical studies or earlier stage clinical trials in subsequent clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.
- We may experience delays in the planned clinical development program for razuprotafib, 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.
- If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.
- Our patents covering one or more of our products or product candidates could be found invalid or unenforceable if challenged.
- If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our products.
- 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 intend to rely on third parties to conduct some or all aspects of our product manufacturing, and these third parties may not perform satisfactorily.
- 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 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.

- 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.

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

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

- 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.

- Changes in tax law may adversely affect us or our investors.

The summary risk factors described above should be read together with the text of the full risk factors below, in the section entitled “Risk Factors” and the other information set forth in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes, as well as in other documents that we file with the Securities and Exchange Commission. The risks summarized above or described in full below are not the only risks that we face. Additional risks and uncertainties not presently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

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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 our strategy, future operations, anticipated financial position, future revenues and projected costs; our strategic alternatives review process and the potential transactions that may be identified and explored as a result of that process; the intended benefits from our collaboration with Gossamer Bio for GB004, including the continued development of GB004 and the milestone and royalty payments related to the collaboration; 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 ability to identify and consummate strategic alternatives that yield additional value for shareholders; the timing, benefits and outcome of our strategic alternatives review process, including the determination of whether or not to pursue or consummate any strategic alternative; the structure, terms and specific risks and uncertainties associated with any potential strategic transaction; potential disruptions in our business and the stock price as a result of our exploration, review and pursuit of strategic alternatives or the public announcement thereof and any decision or transaction resulting from such review; the accuracy of our estimates regarding expense, future revenues, uses of cash, capital requirements and the need for additional financing; the continued development of GB004 and maintaining and deriving the intended benefits of the Company’s collaboration with Gossamer Bio; ability to continue to develop razuprotafib or other product candidates, including in indications related to COVID-19; our review and evaluation of strategic plans for our razuprotafib glaucoma program; 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 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.

Unless the context requires otherwise, references to this Annual Report on Form 10-K to “Aerpio,” the “Company,” “we,” “us,” and “our” refer to Aerpio Pharmaceuticals, Inc. and its subsidiaries, on a consolidated basis.

PART I

Item 1. Business.

Overview

Aerpio Pharmaceuticals, Inc.(“Aerpio” or the “Company”) is a biopharmaceutical company focused on developing compounds that activate Tie2 in indications in which the Company believes that activation of Tie2 may have therapeutic potential. Our product candidates include razuprotafib (formerly known as AKB-9778), a small molecule VE-PTP inhibitor.

In March 2019, we announced topline results from our Phase 2b (“TIME-2b”) clinical trial of AKB-9778 for the treatment of non-proliferative diabetic retinopathy. Although the results did not meet the study’s primary endpoint, we believe that the TIME-2b study further supported the reduction of intraocular pressure (“IOP”) seen with subcutaneous razuprotafib in the previous TIME-2 study. Based on these findings, we developed a topical ocular formulation of razuprotafib, and observed in preclinical studies activation of Tie2 in Schlemm’s canal, IOP reduction via enhanced outflow facility and favorable tolerability.

In June 2019, we initiated a double-masked, multiple-ascending dose Phase 1b clinical trial for open angle glaucoma (“OAG”). We enrolled four cohorts of 12 subjects each and subjects received increasing daily doses of a topical ocular formulation of razuprotafib or placebo for seven days. The primary endpoint of the trial was ocular safety and tolerability, with IOP lowering as the key pharmacodynamic endpoint. Based on the unmasked interim analysis of Phase 1b, limited to the first three cohorts, which showed the topical ocular administration of razuprotafib was well tolerated, and a time and dose dependent reduction in IOP that, in the highest once daily (“QD”) dose cohort peaked at 4 hours post-dose and was sustained through eight hours on day 7, returning to baseline levels at 24 hours post-dose, a cohort of 43 patients with OHT/OAG (hypertensive eyes) was added to the ongoing study to assess safety and pilot efficacy in the target patient population.

In January 2020, we announced the results of the fifth cohort of subjects noting subjects in cohort five randomized to the active arm exhibited statistically significant decreases in IOP at all post razuprotafib administration time points on both days 1 and 7 compared with day -1 baseline values when they were being treated with prostaglandin alone. When the change is placebo-corrected, razuprotafib plus prostaglandin versus prostaglandin alone produced a statistically significant decrease in IOP on Day 7 at 0, 4 and 8 hours post dose as compared to placebo. We believed these results suggested a persistent IOP-lowering activity from adding razuprotafib to standard-of-care prostaglandin therapy. Topical ocular administration of razuprotafib was well tolerated over seven days in cohort five. There were no reports of conjunctival hemorrhage or pain on instillation during the seven days of dosing and no systemic/non-ocular AEs were observed.

In June 2020, we initiated a Phase 2 clinical trial designed to evaluate the safety and efficacy of a topical formulation of razuprotafib in approximately 195 patients followed over a 28-day period. Patients enrolled in the trial were administered a baseline of latanoprost ophthalmic solution 0.005%, and then randomized in a 1:1:1 fashion to receive adjunctive therapy consisting of placebo, 40 mg/ml razuprotafib once-daily, or 40 mg/ml razuprotafib twice-daily. The primary endpoint of the study was mean diurnal IOP at 28 days in the razuprotafib treated groups compared to the latanoprost monotherapy group.

In December 2020, we reported that razuprotafib met the primary efficacy endpoint at Day 28 with the twice-daily (“BID”) dose group in Aerpio’s double-blind, placebo-controlled Phase 2 trial in patients with elevated IOP associated with OAG or OHT. The change from baseline in diurnal mean IOP at Day 28 of study eyes treated with razuprotafib BID plus latanoprost showed a statistically significant improvement, or drop in IOP, (two-sided p-value 0.0130 and LS mean difference of -0.92 mm Hg) compared to those treated with latanoprost monotherapy. The razuprotafib QD dose group did not show a statistically significant improvement at Day 28. Further analysis of the results demonstrated that razuprotafib had a larger IOP reduction after longer duration dosing (28 days versus 14 days) consistent with its potential mechanism of repairing Schlemm’s canal. Razuprotafib also produced larger IOP reductions in patients with higher starting IOP, or a 1.6 mm Hg IOP reduction in patients with post wash-out IOP’s of >26 mm Hg and the topical drops were well tolerated in this trial. While the trial met the primary efficacy endpoint at Day 28 with the BID group, the IOP decrease was not at a level deemed sufficient to move to Phase 3 development.

Following the announcement regarding the topline results from the Phase 2 clinical trial of razuprotafib in patients with elevated IOP associated with OAG or OHT, the Company initiated a process to explore a range of strategic alternatives focused on maximizing stockholder value from our clinical and preclinical assets and cash resources. As part of this process, we are exploring strategic options for partnering our programs, as well as the potential for an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. Ladenburg Thalmann & Co. Inc. and Duane Nash, M.D., J.D., M.B.A, continue to be retained with respect to the strategic review process. There can be no assurance that this exploration of strategic alternatives will result in the Company entering or completing any transaction.

Additionally, in January 2021, the Company initiated a realignment plan to reduce operating costs and better align its workforce with the needs of its ongoing business. The realignment plan reduces its current workforce by 7 employees, representing approximately 58% of our workforce. As a result of this realignment plan, we estimate we will incur one-time employee related severance expenses of approximately $1.2 million in the first quarter of 2021. We anticipate the majority of the one-time employee severance liability to be paid during 2021. Each affected employee's eligibility for such severance benefits is contingent upon such employee's execution of a separation agreement, which includes a general release of claims against us. The charges that we expect to incur in connection with the realignment plan are subject to a number of assumptions, and actual results may differ from our original estimate. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the realignment plan.

Other assets in our pipeline include the following:

Acute Respiratory Distress Syndrome

Based on results in preclinical studies and observations in patients in TIME-2 and TIME-2b trials, we believe that a vascular endothelial receptor, Tie2, may play a pivotal role in the defense against microvascular breach in ARDS. We hypothesize that razuprotafib may have therapeutic potential for the treatment of COVID-19 associated ARDS and initiated two Phase 2 trials during 2020.

Quantum Leap Healthcare Collaboration I-SPY COVID Trial

In May 2020, we were selected by Quantum Leap Healthcare Collaborative to participate in the I-SPY COVID Trial (Investigation of Serial studies to Predict Your COVID Therapeutic Response with biomarker Integration and Adaptive Learning) to evaluate subcutaneous razuprotafib for the treatment of COVID-19 related ARDS in adult patients with critical COVID-19 (ClinicalTrials.gov Identifier: NCT04488081). The trial was initiated during the third quarter of 2020 but in January 2021, the Data Monitoring Committee recommended discontinuation of razuprotafib after 21 patients due to the complexity of monitoring patients in the setting of a surge in ICU patients. There were no apparent safety signals associated with razuprotafib in these 21 patients and we believe the scientific basis is sound for continuing to evaluate the drug in patients presenting with ARDS across a broader array of infections.

MTEC RESCUE COVID Trial

In August 2020, we announced the receipt of funding to evaluate subcutaneous razuprotafib in a new randomized, investigational trial for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 ("RESCUE" trial; ClinicalTrials.gov Identifier: NCT04511650). The RESCUE trial will evaluate subcutaneous razuprotafib for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 as part of the MTEC-20-09-COVID-19 Treatment Military Infectious Disease Research Program ("MIDRP"). The Medical Technology Enterprise Consortium ("MTEC"), a non-profit organization primarily funded by the U.S. Army Medical Research and Development Command, will provide up to $5.1 million of reimbursement related to qualified internal and external spending, as it relates to the clinical trial. The RESCUE clinical trial was initiated during the third quarter of 2020 but we decided to stop recruiting in February 2021 after the first 31 patients were enrolled based on challenges recruiting and monitoring patients in the current pandemic environment. There were no apparent safety signals associated with dosing COVID-19 patients in the RESCUE trial and we plan to further analyze the data to assess trends in efficacy and biomarkers. We expect to report top-line data in the second quarter of 2021.

Diabetic Kidney Disease

In two consecutive trials, TIME-2 and TIME-2b, subcutaneous AKB-9778 showed reduction in Urine Albumin-Creatinine Ratio ("UACR"), a measure of progression of diabetic kidney disease. In a post-hoc analysis of the earlier TIME-2 clinical trial, there was a 21% reduction (geometric mean) in UACR from baseline in the AKB-9778 treatment arms, but an overall increase in UACR in the placebo arm. The prospective UACR analyses from the recently completed TIME-2b trial largely replicated the results from the previous trial and reinforced the potential beneficial effects of Tie2 activation in diabetic kidney disease. 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.

ARP-1536 and Bispecific Antibody

ARP-1536, our humanized monoclonal antibody directed at the same target as subcutaneous razuprotafib, is in preclinical development. We are evaluating development options for ARP-1536, including subcutaneous injection for the treatment of diabetic vascular complications, e.g., diabetic nephropathy and intravitreal injection as an adjunctive therapy for diabetic macular edema. We are also developing a bispecific antibody that binds both vascular endothelial growth factor ("VEGF") and vascular endothelial protein tyrosine phosphatase ("VE-PTP") which is designed to inhibit VEGF activation and activate Tie2. We believe this bispecific antibody has the potential to be an improved treatment for wet AMD and diabetic macular edema via intravitreal injection.

Gossamer License Agreement

In June 2018, we licensed AKB-4924, a selective stabilizer of hypoxia-inducible factor-1 alpha ("HIF-1 alpha") to Gossamer Bio, Inc. ("Gossamer") AKB-4924, (now called GB004), is being developed for the treatment of inflammatory bowel disease ("IBD"). HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. After completing a 28-day Phase 1b study in ulcerative colitis patients during 2020, Gossamer initiated a 12-week Phase 2 study of GB004 in patients with mild-to-moderate ulcerative colitis during the second half of 2020 and expects to report top-line results from this study in the first half of 2022. Gossamer is responsible for all remaining development and commercial activities for GB004.

Our Strategy

Our objective is to develop and advance compounds that activate Tie2 to treat ocular diseases and diabetic complications. We are taking the following critical steps to achieve this goal:

- **Explore strategic collaborations with leading organizations for the development and commercialization of promising product candidates in our pipeline**

  The Company initiated a process to explore a range of strategic alternatives focused on maximizing stockholder value from our clinical assets and cash resources. As part of this process, we are exploring strategic options for partnering our programs, as well as the potential for an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. Ladenburg Thalmann & Co. Inc. and Duane Nash, M.D., J.D., M.B.A, continued to be retained with respect to the strategic review process. There can be no assurance that this exploration of strategic alternatives will result in the Company entering or completing any transaction.

- **Investigate the sale, licensing or partnering of razuprotafib**

  While we elected not to advance razuprotafib into Phase 3 development ourselves, we believe the candidate may nevertheless have therapeutic potential in OAG, and we intend to explore strategic opportunities with third parties.

  In addition, based on results in preclinical studies and observations in patients in TIME-2 and TIME-2b trials, we believe that a vascular endothelial receptor, Tie2, may play a pivotal role in the defense against microvascular breach in ARDS or potentially across a broader array of infections beyond COVID-19.

Additionally, the downregulation of Tie2 activity occurs in the vasculature of diabetics systemically, particularly in the kidney. In a post-hoc analysis of the earlier TIME-2 clinical trial, there was a 21% reduction (geometric mean) in UACR from baseline in the razuprotafib treatment arms, but an overall increase in UACR in the placebo arm. The prospective UACR analyses from the recently completed TIME-2b trial largely replicated the results from the previous trial and reinforced the potential beneficial effects of Tie2 activation in diabetic kidney disease. Based on the confirmation of decreased of UACR, a potential indicator of improved kidney function, in the completed TIME-2b trial, we are exploring strategic options for further development of razuprotafib for other indications.

- **Explore strategic options for further development of ARP-1536 and the Bispecific antibody**

  We are exploring strategic options for further development of ARP-1536, including subcutaneous injection for the treatment of diabetic vascular complications including nephropathy and intravitreal injection for the adjunctive treatment of diabetic macular edema. We are also exploring development options for the bispecific antibody as a potential treatment for wet AMD and DME via intravitreal injection.

- **Focus on cash management to preserve cash**

  In January 2021, we initiated a realignment plan to reduce operating costs and better align its workforce with the needs of our ongoing business. The realignment plan, reduces its current workforce by 7 employees, representing approximately 58% of our workforce. As a result of this realignment plan, we estimate we will incur one-time employee related severance expenses of approximately $1.2 million in the first quarter of 2021. We anticipate the majority of the one-time employee severance liability to be paid during 2021.

Razuprotafib in Open Angle Glaucoma

Unmet Medical Need:

OAG 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. OAG is characterized by optic nerve and neuroretina anomalies and progressive visual field defects. Elevated intraocular pressure ("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 OAG. Importantly, most current OAG 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 OAG 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 OAG. 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 OAG. 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 OAG therapy.

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

Aerpio has developed potent and selective small molecule inhibitors of the catalytic domain of vascular endothelial protein tyrosine phosphatase (VE-PTP). In vascular endothelial cells, razuprotafib, 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 ("eNOS") activation and Rho pathway inhibition via Rac1. In preclinical studies in mice, topical ocular razuprotafib activated Tie2 in Schlemm's canal, increased Schelmm's canal area and reduced IOP via enhanced outflow. Taken together these results indicate the razuprotafib reduces IOP via a novel and potentially disease modifying Tie2 mediated effect on Schlemm's canal and conventional outflow.

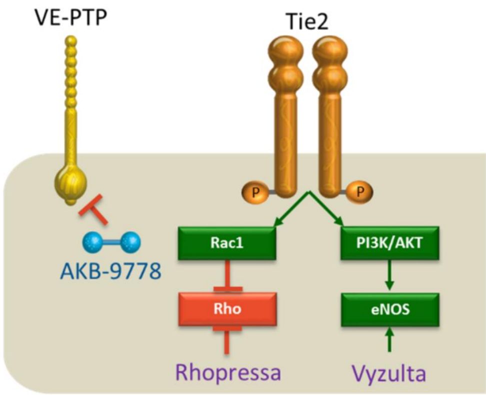

Figure 1. VE-PTP inhibition as a novel conventional outflow targeted approach for glaucoma treatment

Activation of Tie2, with razuprotafib, 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.

Clinical Results in OAG

The results of our Phase 2b ("TIME-2b") clinical trial showed encouraging data demonstrating the potential for razuprotafib to reduce intraocular pressure in open angle glaucoma and ocular hypertension. In June 2019, we initiated a double-masked, multiple-ascending dose Phase 1b trial and enrolled four cohorts of 12 subjects each. Subjects received increasing daily doses of a topical ocular formulation of razuprotafib or placebo for seven days. The primary endpoint of the trial was ocular safety and tolerability, with IOP lowering as the key pharmacodynamic endpoint. In October 2019, we announced interim results from our Phase 1b clinical trial. The unmasked interim analysis, limited to the first three cohorts, showed the topical ocular administration of razuprotafib was well tolerated. Compared to placebo, there was a dose dependent increase in minimal to mild conjunctival hyperemia with razuprotafib, which was transient and generally considered non-adverse, and a time and dose dependent reduction in IOP that, in the highest QD dose cohort peaked at 4 hours post-dose and was sustained through eight hours on day 7, returning to baseline levels at 24 hours post-dose. Based on these data, a fifth cohort of 43 patients was recruited with OHT/POAG and baseline IOP measurements between 17 and 27 mmHg while treated with once-daily prostaglandin therapy. Patients were randomized 3:1 to receive either razuprotafib (32 subjects) or placebo (11 subjects), administered in the morning for 7 days, while continuing their evening prostaglandin therapy. Conjunctival hyperemia, IOP, safety and pilot efficacy were assessed in the same manner as described for cohorts one to four.

In January 2020, we announced the results of the fifth cohort of subjects noting subjects in cohort five randomized to the active arm exhibited statistically significant decreases in IOP at all post- razuprotafib administration time points on both days 1 and 7 compared with day -1 baseline values when they were being treated with prostaglandin alone.

Topical ocular administration of razuprotafib was well tolerated over seven days in cohort five. In the active arm treated with razuprotafib plus prostaglandin, 21.9% of subjects experienced hyperemia compared with 9.1% of subjects in the prostaglandin-alone arm. In all cases, this hyperemia was minimal-to-mild in severity, transient in duration and generally considered non-adverse. There were no reports of conjunctival hemorrhage or pain on instillation during the seven days of dosing and no systemic/non-ocular AEs were observed.

We initiated a Phase 2 clinical trial during the second quarter of 2020 designed to evaluate the safety and efficacy of a topical formulation of razuprotafib in approximately 195 patients followed over a 28-day period. Patients enrolled in the trial were administered a baseline of latanoprost ophthalmic solution 0.005%, and then randomized in a 1:1:1 fashion to receive adjunctive therapy consisting of placebo, 40 mg/ml razuprotafib once-daily, or 40 mg/ml razuprotafib twice-daily. The primary endpoint of the study was mean diurnal IOP at 28 days in the razuprotafib treated groups compared to the latanoprost monotherapy group.

In December 2020, we reported that razuprotafib met the primary efficacy endpoint at Day 28 with the twice-daily ("BID") dose group in Aerpio's double-blind, placebo-controlled Phase 2 trial in patients with elevated IOP associated with OAG or OHT. The change from baseline in diurnal mean IOP at Day 28 of study eyes treated with razuprotafib BID plus latanoprost showed a statistically significant improvement, or drop in IOP, (two-sided p-value 0.0130 and LS mean difference of -0.92 mm Hg) compared to those treated with latanoprost monotherapy. The razuprotafib once-daily ("QD") dose group did not show a statistically significant improvement at Day 28. Further analysis of the results demonstrated that razuprotafib had a larger IOP reduction after longer duration dosing (28 days versus 14 days) consistent with its potential mechanism of repairing Schlemm's canal. Razuprotafib also produced larger IOP reductions in patients with higher starting IOP, or a 1.6 mmHg IOP reduction in patients with post wash-out IOP's of >26 mmHg. The razuprotafib topical drops were well tolerated in this trial. While the trial met the primary efficacy endpoint at Day 28 with the BID group, the IOP decrease was not at a level deemed sufficient to move to Phase 3 development.

Role of Tie2 Mediated Vascular Stabilization in Diabetic Vascular Complications and in ARDS/COVID-19

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 and in patients COVID-19, an upregulation of VE-PTP an enzyme that inactivates Tie2, may contribute to vascular destabilization.

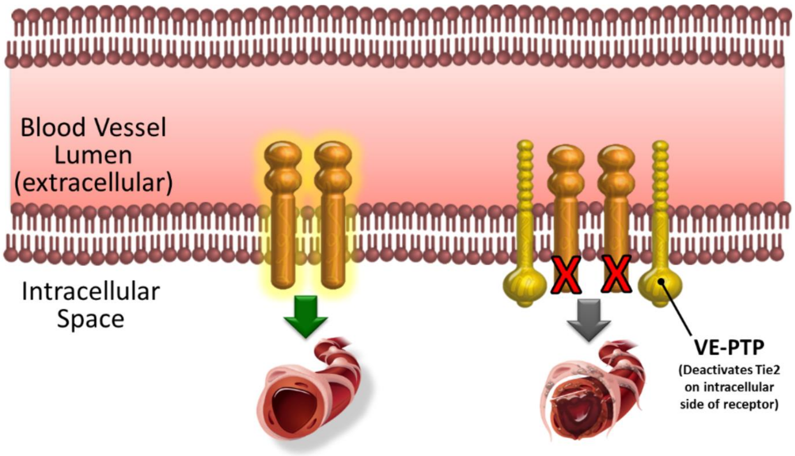

Figure 2. VE-PTP is upregulated in diabetic vasculature and in hypoxic endothelial cells which is common in patients with ARDS, leading to deactivation of the Tie2 receptor

Razuprotafib

Razuprotafib works by inhibiting VE-PTP, an enzyme that is upregulated in diabetic vasculature and hypoxic endothelial cells and that is responsible for inactivating Tie2. Razuprotafib 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 razuprotafib minimize the potential for off-target side effects. Inhibition of the inhibitor, VE-PTP, by razuprotafib leads to activation of Tie2.

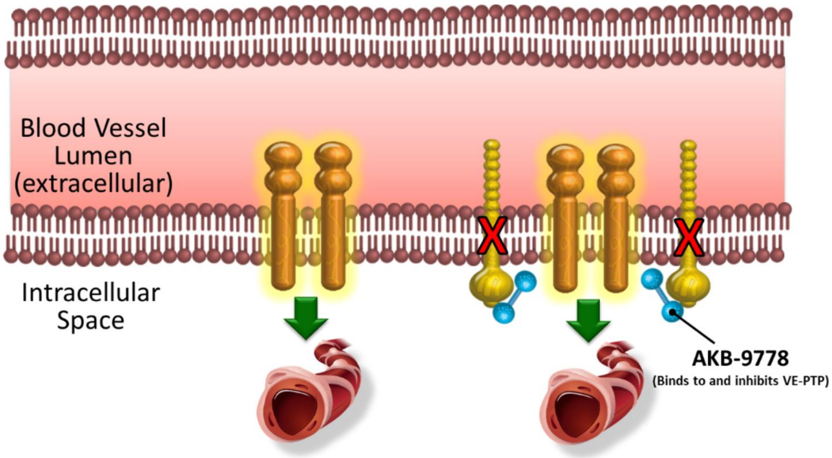

Figure 4. Razuprotafib binds to and inhibits the active site of VE-PTP, resulting in Tie2 activation

We are aware that Roche is developing agents that inhibit Angpt-2, a natural antagonist of Tie2. Angpt-2 can bind to Tie2 and prevent Angpt-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 Angpt 1/2 binding.

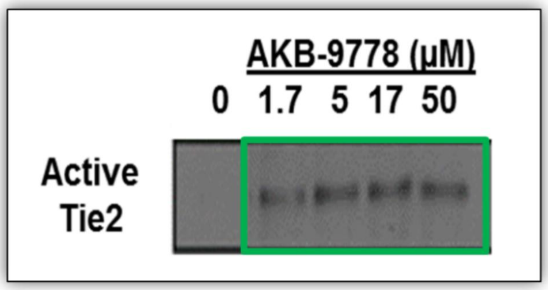

Figure 3. Inhibiting VE-PTP with razuprotafib robustly activates Tie2 in human endothelial cells in pre-clinical experiments (Shen et al. JCI 124:4564-76, 2014)

Role of Tie2 in ARDS in COVID-19 Infections

Preclinical models, large human observational studies, and human genetic studies from leading groups worldwide have independently arrived at the concept that a vascular endothelial receptor, Tie2, may play a pivotal role in the defense against microvascular breach in ARDS. We hypothesize that razuprotafib, being developed as a Tie2 activating compound, could exhibit an acceptable safety profile and show therapeutic promise in the treatment of COVID-19 associated ARDS as a potentially life-saving therapeutic for patients suffering from the devasting respiratory effects of COVID-19.

Starting in 2020, we initiated two Phase 2 clinical trials in COVID-19 patients. One with Quantum Leap Healthcare Collaborative to participate in the I-SPY COVID Trial (Investigation of Serial studies to Predict Your COVID Therapeutic Response with biomarker Integration and Adaptive Learning) to evaluate subcutaneous razuprotafib for the treatment of COVID-19 related ARDS in adult patients with critical COVID-19 and one with the military, called RESCUE, to evaluate subcutaneous razuprotafib for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 as part of the MTEC-20-09-COVID-19 Treatment Military Infectious Disease Research Program ("MIDRP").

The I-SPY COVID platform trial includes a study arm that evaluated razuprotafib's potential to sufficiently stabilize the pulmonary vasculature, in order to slow or prevent the progression of COVID-19 associated pulmonary pathology, decrease the need for ventilator support, and reduce mortality. The I-SPY COVID study of razuprotafib was stopped after 21 patients in January 2021 due to the complexity of monitoring patients in the setting of a surge in ICU patients. There were no apparent safety signals associated with razuprotafib in these 21 patients and we believe the scientific basis is sound for continuing to evaluate the drug in patients presenting with ARDS across a broader array of infections.

In the military sponsored RESCUE trial, we are evaluating razuprotafib for the potential to exhibit an acceptable safety profile and show efficacy for treatment of ARDS in patients with moderate to severe COVID-19; potentially being a life-saving therapeutic for service members in the field suffering from the devasting respiratory and vascular effects of COVID-19. The RESCUE clinical trial was initiated during the third quarter of 2020 but in February 2021, we decided to stop recruiting after the first 31 patients were enrolled based on challenges recruiting and monitoring patients in the current pandemic environment. There were no apparent safety signals associated with dosing COVID-19 patients in the RESCUE trial and we plan to further analyze the data to assess trends in efficacy and biomarkers. We expect to report top-line data in the second quarter of 2021.

Other Potential Systemic Indications – Diabetic Nephropathy

Systemic therapy with razuprotafib could also provide therapeutic benefits in other areas of the body affected by diabetes, including in the kidneys and other organ systems. 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. Razuprotafib showed encouraging data in a number of prespecified, key secondary endpoints, consistent with the observations in the prior Phase 2a ("TIME-2") trial related to the changes in UACR, a measure of kidney function. In a post-hoc analysis of the earlier TIME-2 clinical trial, there was a 21% reduction (geometric mean) in UACR from baseline in the razuprotafib treatment arms, but an overall increase in UACR in the placebo arm. The prospective UACR analyses from the recently completed TIME-2b trial largely replicated the results from the previous trial and reinforced the potential beneficial effects of Tie2 activation in diabetic kidney disease.

ARP-1536

ARP-1536 is a humanized monoclonal antibody currently in preclinical development that is directed at the same target as subcutaneous razuprotafib. 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 razuprotafib. We are evaluating development options for ARP-1536, including subcutaneous injection for the treatment of diabetic vascular complications, e.g. diabetic nephropathy and intravitreal injection as an adjunctive therapy for diabetic macular edema.

Bi-specific Antibody

We are also developing a bispecific antibody that binds both VEGF and VE-PTP which is designed to inhibit VEGF activation and activate Tie2. Our bispecific antibody is differentiated because it directly activates Tie2 and inhibits VEGF activation. The novel bimodal activity has been observed in a variety of cell-based models. The antibody has shown activity in animal models of retinal disease. We believe this bispecific antibody has the potential to be an improved treatment for wet AMD and diabetic macular edema via intravitreal injection.

License Agreement with Gossamer

In June 2018, we entered into a license agreement (the "Gossamer License Agreement") with a wholly-owned subsidiary of Gossamer, under which we granted Gossamer an exclusive, sublicensable license to develop and commercialize AKB-4924 (now called GB004) and other structurally related products worldwide, with initial development expected in the indications of induction and maintenance in ulcerative colitis and Crohn's Disease (collectively "initial indications"). GB004, a selective stabilizer of HIF-1 alpha, works by inhibiting HIF prolylhydroxylase enzymes. Unlike other compounds currently in development that act broadly against all forms of HIF, GB004 selectively stabilizes a specific form of HIF, HIF-1 alpha. HIF-1 alpha has an effect on innate immunity and epithelial barrier function. However, HIF-1 alpha differs from HIF-2, in that it does not stimulate the formation of new red blood cells. Gossamer reported topline results from the Phase 1b study in ulcerative colitis patients in the second quarter of 2020 and announced, subject to developments in the ongoing COVID-19 pandemic, it initiated a 12-week Phase 2 study of GB004 in patients with mild-to-moderate ulcerative colitis during the second half of 2020. Gossamer is expected to have results of the Phase 2 study in ulcerative colitis patients in the first half of 2022.

Gossamer is responsible for the further development and commercialization of the licensed products, and a joint development committee has been formed to oversee the development and manufacturing activities related to the licensed products.

On May 12, 2020, the Company entered into Amendment No. 1 to the Gossamer License Agreement ("Amendment No. 1"). Pursuant to Amendment No. 1, Gossamer made a payment to the Company of $15.0 million on May 12, 2020. For the year ended December 31, 2020, the Company recognized revenue of $15.0 million based on the terms of Amendment No. 1. No such revenue was recognized during the year ended December 31, 2019.

Under the terms of the Gossamer License Agreement and as amended by Amendment No. 1 (collectively, the "Amended Gossamer License Agreement"), Gossamer is obligated to use its commercially reasonable efforts to develop and commercialize licensed products in the United States, two major European countries and Japan for at least one of the initial indications. The Amended Gossamer License Agreement includes an exclusivity provision that prohibits us from developing, manufacturing or commercializing, and prohibits Gossamer from clinically developing or commercializing certain HIF stabilizing compounds other than as permitted in the Amended Gossamer License Agreement.

Under the terms of the Amended Gossamer License Agreement, we are eligible to receive up to $40.0 million in approval milestone payments related to indications in ulcerative colitis and Crohn's disease, and up to $50.0 million in sales milestone payments. The Company is also eligible to receive the tiered royalties on sales of licensed products from percentages ranging from a low-single-digit to mid-single-digit, subject to certain customary reductions.

In addition, under certain circumstances, in lieu of receiving the foregoing milestone payments and royalties, the Company may elect to receive 20% of payments received by Gossamer and its stockholders (with some exclusions) in connection with Gossamer's grant of a sublicense or other rights to the licensed products or if Gossamer undergoes a change of control and the value of the transaction exceeds a certain value (provided that Gossamer can prevent the Company from exercising this option if the parent company of Gossamer is the entity undergoing the change of control, in which case each of the royalty rate percentages described above would automatically be increased by low single digits). Conversely, the Company could be required to accept such 20% of those payments if Gossamer agrees to pay the Company a certain minimum upon Gossamer and its stockholders being paid. Such amount may be reduced if the transaction includes pharmaceutical candidates or products or other named asset categories in addition to the licensed products.

The Amended Gossamer License Agreement expires on a licensed-product-by-licensed-product and country-by-country basis on the later of fifteen years from the date of first commercial sale or when there is no longer a valid patent claim covering such licensed product in such country. Either party may terminate the Amended Gossamer License Agreement for an uncured material breach by the other party or upon the bankruptcy or insolvency of the other party. Gossamer may terminate the Amended Gossamer License Agreement in the event Gossamer determines there is a potential safety or efficacy issue with the licensed products. We may terminate the Amended Gossamer License Agreement if Gossamer institutes certain actions related to the licensed patents. Under certain termination circumstances, we would have worldwide rights to the terminated program.

As of December 31, 2020 and 2019, all development milestones, sales-based milestones and royalty payments within the Amended Gossamer License Agreement are constrained to the point where no transaction price has been allocated to the future milestones or royalty payments.

Intellectual Property

As of December 31, 2020, we owned at least 40 U.S. patents, at least 32 pending U.S. provisional or non-provisional patent applications, at least 286 foreign patents and at least 94 pending foreign applications, with claims directed toward various aspects of our product candidates and research programs, not counting patents and patent applications that have been licensed to a third party. 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 2041, without taking into account any possible patent term adjustments or extensions. Within the foregoing patent portfolio, as of December 31, 2020, we owned at least 10 U.S. patents, at least 7 pending U.S. provisional or non-provisional patent applications, at least 52 foreign patents and at least 32 pending foreign applications that are directed toward ARP-1536 and formulations or uses thereof. As of December 31, 2020, within the foregoing patent portfolio, we owned at least 30 U.S. patents, at least 25 pending U.S. provisional or non-provisional patent applications, at least 234 foreign patents and at least 62 pending foreign applications that are directed toward razuprotafib and formulations, 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 razuprotafib are set to expire in 2027, 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.

Sales and Marketing

We hold worldwide commercialization rights to all of our product candidates. We are evaluating our development options for our product candidates and, if any receive marketing approval, we may seek to commercialize such candidates independently or in collaboration with one or more third parties.

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. 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 ("FDCA") and its implementing regulations, and biologics under the FDCA and the Public Health Service Act ("PHSA") and its implementing regulations. FDA approval is required before any new unapproved drug or biologic, 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, voluntary or mandatory 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 ("GLP") regulations;
- submission to the FDA of an investigational new drug application ("IND") which must become effective before human clinical trials may begin and must be updated annually;
- approval by an independent institutional review board ("IRB") or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practices ("GCPs") 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 ("BLA") or a new drug application ("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 ("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 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.

Preclinical Studies

Before testing any drug or biologic in humans, the product candidate must undergo rigorous preclinical, or nonclinical, testing. Preclinical studies include laboratory evaluations of chemistry, formulation and stability, as well as *in vitro* and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety and toxicology studies. In the United States, the results of the preclinical studies, together with manufacturing information and analytical data must be submitted to the FDA as part of an IND.

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 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 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 investigational product is initially introduced into a limited population of 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 product candidates), to evaluate the overall benefit-risk profile of the investigational product, and to provide an adequate basis for physician labeling. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA or NDA.
- *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. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products.

Sponsors must also submit progress reports detailing the results of the clinical trials, among other information, at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators 15 days after the trial sponsor determines the information qualifies for reporting for 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. Sponsors must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reactions as soon as possible but in no case later than 7 calendar day after the sponsor's initial receipt of the information.

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.

A manufacturer of an investigational drug or biological product for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug or biological product. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy.

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 2020, the application user fee is $2,942,965, and the sponsor of an approved BLA or NDA is also subject to an annual program fee of $325,424 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 BLAs and NDAs 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 (“REMS”) program 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 or biologic 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, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug or biologic 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. The benefits of Breakthrough Therapy Designation include the same benefits as a Fast Track Designation, in addition to intensive guidance from FDA to ensure an efficient product development program.

Post-Approval Requirements

Drugs and biologics 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 and biologic 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.

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 may 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. FDA has authority to require post-market studies, in certain circumstances, on reduced effectiveness of a drug or biologic and FDA may require labeling changes related to new reduced effectiveness information. Other potential consequences of a failure to maintain regulatory compliance include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- mandated modification of promotional materials and labeling and issuance of corrective information;
- 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;
- injunctions or the imposition of civil or criminal penalties; or
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs.

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 ("PSP") within 60 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. Generally, 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 ("Affordable Care Act") signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("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 ("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 ("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 ("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.

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. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension of clinical trials, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

European Union Clinical Trials Regulation

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 ("CTA"), must be submitted for each clinical protocol to each country's National Competent Authority, or NCA, and at least one independent Ethics Committee, or EC, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical trial may proceed. Under the current regime (the EU Clinical Trials Directive 2001/20/EC and corresponding national laws) all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the NCA and ECs of the Member State where they occurred.

In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It will overhaul the current system of approvals for clinical trials in the European Union. Specifically, the new regulation, which will be directly applicable in all Member States (meaning that no national implementing legislation in each European Union Member State is required), aims at simplifying and streamlining the approval of clinical trials in the European Union. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single entry point and strictly defined deadlines for the assessment of clinical trial applications. It is expected that the new Clinical Trials Regulation (EU) No 536/2014 will come into effect following confirmation of full functionality of the Clinical Trials Information System, the centralized European Union portal and database for clinical trials foreseen by the new Clinical Trials regulation, through an independent audit, which is currently expected to occur in December 2021.

Drug Review and Approval in Europe

In the European Economic Area (comprised of the Member States of the European Union plus Norway, Iceland, and Lichtenstein), or EEA, medicinal products are subject to extensive pre- and post-market regulation by regulatory authorities at both the EEA and national levels. Before being placed on the market in the UK or EEA, a medicinal product requires a marketing authorization from the relevant competent authority.

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

- *Centralized procedure.* The European Medicines Agency ("EMA"), implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the EEA. 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, designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue-engineered products) and 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 viral diseases.
- 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 contains a new active substance or

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 EEA countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:
- *Decentralized procedure.* Under the decentralized procedure, an applicant may apply for simultaneous authorization in more than one EEA country of medicinal products that have not yet been authorized in any EEA 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 EEA Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other EEA countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

Now that the United Kingdom (which comprises Great Britain and Northern Ireland) has left the European Union, Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the United Kingdom medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required.

Companies developing a new medicinal product must also agree upon, a Pediatric Investigation Plan ("PIP") with the EMA's Pediatric Committee ("PDCO"), and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies, (e.g., because the relevant disease or condition occurs only in adults). A PIP describes, among other things, proposed pediatric trials and their timing relative to clinical trials in adults. The marketing authorization application for the product must include the results of pediatric clinical trials conducted in accordance with the PIP, unless a waiver applies, or a deferral has been granted by the PDCO of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults, in which case the pediatric clinical trials must be completed at a later date. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP are eligible for a six month extension of the protection under a supplementary protection certificate (if any is in effect at the time of approval) even where the trial results are negative. In the case of orphan medicinal products, a two year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted

Data and Marketing Exclusivity

In the EEA, innovative medicinal products qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's pre-clinical or clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization for a period of eight years from the date on which the reference product was first authorized in the EEA. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. 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. Even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on a marketing authorization application with a completely independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Accelerated Review

Under the centralized procedure in the EEA, the maximum timeframe for the evaluation of a marketing authorization application is 210 days from receipt of a valid application (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 ("CHMP"). Clock stops may extend the timeframe of evaluation of a marketing authorization application considerably beyond 210 days. 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. If the CHMP accepts such a request, the timeframe of 210 days for assessment will be reduced to 150 days (excluding clock stops), but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). Thereafter, in March 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty, and the United Kingdom formally left the European Union on January 31, 2020. A transition period began on February 1, 2020, during which European Union pharmaceutical law remained applicable to the United Kingdom, however this ended on December 31, 2020. Since the regulatory framework in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union Directives and Regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom, as United Kingdom legislation now has the potential to diverge from EU legislation. It remains to be seen how Brexit will impact regulatory requirements for product candidates and products in the United Kingdom in the long-term. The MHRA, the UK medicines and medical devices regulator, has recently published detailed guidance for industry and organizations to follow from January 1, 2021 now the transition period is over, which will be updated as the UK's regulatory position on medicinal products evolves over time.

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, including 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 ("ACA") 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. Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court; the Trump Administration had issued various Executive Orders which eliminated cost sharing subsidies and various provisions 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; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. As implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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, overtly or covertly, in cash or in kind, 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties statute. Violations of the AKS carry potentially significant civil and criminal penalties, including imprisonment, fines, administrative civil monetary penalties, and exclusion from participation in federal healthcare programs.
- The federal anti-inducement law which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program;
- Federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act ("FCA") which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.
- The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and its implementing regulations, which prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

- HIPAA, as amended by the Health Information Technology and Clinical Health Act ("HITECH") and its implementing regulations, which imposes certain requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses, otherwise known as covered entities, relating to the privacy, security and transmission of individually identifiable health information, including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The federal transparency requirements under the Affordable Care Act, including the Physician Payment Sunshine Act, which require drug and biologics manufacturers eligible for payment under Medicare, Medicaid or the Children's Health Insurance Program to report annually to HHS, information related to payments or other "transfers of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- State and foreign 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 ("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 administrative, 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 and Human Capital

As of December 31, 2020, we had 12 full-time or part-time employees, including five employees with doctorate level degrees. Of these employees, six employees are engaged in research and development activities and six 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.

In January 2021, the Company initiated a realignment plan to reduce operating costs and better align its workforce with the needs of its ongoing business. The realignment plan reduces its current workforce by 7 employees, representing approximately 58% of our workforce. As a result of this realignment plan, we estimate we will incur one-time employee related severance expenses of approximately $1.2 million in the first quarter of 2021. We anticipate the majority of the one-time employee severance liability to be paid during 2021.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees, advisors and consultants. The principal purposes of our equity incentive plans are to attract, retain and reward personnel through the granting of equity-based compensation awards in order to increase shareholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Our Corporate Information

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

Our corporate headquarters are located at 9987 Carver Road Suite 420, Cincinnati, Ohio 45242, and our telephone number is (513) 985-1920. We maintain a website at www.aerpio.com, to which we regularly post copies of our press releases as well as additional information about us. Our filings with the Securities and Exchange Commission (the “SEC”) will be available free of charge through the website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. Information contained in our website does not constitute a part of this Annual Report on Form 10-K or any of our other filings with the SEC unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC’s Interactive Data Electronic Applications system at http://www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

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 4 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 Business and the Clinical Development, Regulatory Review and Approval of Product Candidates

Risks Related to Our Evaluation of Strategic Alternatives

We cannot assure you that our exploration of strategic alternatives will result in a transaction or that any such transaction would be successful, and the process of exploring strategic alternatives or its conclusion could adversely impact our business and our stock price.

In October 2019, we announced the engagement of Evercore, Ladenburg Thalmann & Co. Inc. and Duane Nash, M.D., J.D., M.B.A. to assist us in identifying and evaluating a range of potential strategic alternatives, including an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. This strategic alternative process is ongoing and, as announced in January 2021, we continue to engage Ladenburg Thalmann & Co. Inc. and Duane Nash to assist us with this process. There can be no assurances that the strategic alternatives process will result in the announcement or consummation of any strategic transaction, or that any resulting plans or transactions will yield additional value for shareholders. Any potential transaction would be dependent on a number of factors that may be beyond our control, including, among other things, market conditions, industry trends, the interest of third parties in a potential transaction with us and the availability of financing to potential buyers on reasonable terms.

The process of exploring strategic alternatives could adversely impact our business, financial condition and results of operations. We could incur substantial expenses associated with identifying and evaluating potential strategic alternatives, including those related to equity compensation, severance pay and legal, accounting and financial advisory fees. In addition, the process may be time consuming and disruptive to our business operations, could divert the attention of management and the Board of Directors from our business, could negatively impact our ability to attract, retain and motivate key employees, and could expose us to potential litigation in connection with this process or any resulting transaction. Further, speculation regarding any developments related to the review of strategic alternatives and perceived uncertainties related to the future of the Company could cause our stock price to fluctuate significantly.

If we do not successfully consummate a strategic transaction, our Board of Directors may decide to pursue a dissolution and liquidation of our company. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

There can be no assurance that the process to identify a strategic transaction will result in a successfully consummated transaction. If no transaction is completed, our Board of Directors may decide to pursue a dissolution and liquidation of our Company. In such an event, the amount of cash available for distribution to our shareholders will depend heavily on the timing of such decision and, ultimately, such liquidation, since the amount of cash available for distribution continues to decrease as we fund our operations while we evaluate our strategic alternatives. In addition, if our Board of Directors were to approve and recommend, and our shareholders were to approve, a dissolution and liquidation of our Company, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our shareholders. Our commitments and contingent liabilities may include (i) obligations under our employment and related agreements with certain employees that provide for severance and other payments following a termination of employment occurring for various reasons, including a change in control of our Company; (ii) potential litigation against us, and other various claims and legal actions arising in the ordinary course of business; and (iii) non-cancelable facility lease obligations. As a result of this requirement, a portion of our assets may need to be reserved pending the resolution of such obligations. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation of our Company. If a dissolution and liquidation were pursued, our Board of Directors, in consultation with its advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of our common stock could lose all or a significant portion of their investment in the event of a liquidation, dissolution or winding up of our company.

Risks Related to the COVID-19 Pandemic

The current pandemic of COVID-19 and the future outbreak of other highly infectious or contagious diseases could seriously harm our research, development and potential future commercialization efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.

Broad-based business or economic disruptions could adversely affect our ongoing or planned research and development activities. For example, in December 2019, an outbreak of a novel strain of coronavirus originated in Wuhan, China, and has since spread to other regions and countries worldwide. In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic, and the U.S. government-imposed travel restrictions on travel between the United States, Europe and certain other countries. To date, the COVID-19 pandemic has caused significant disruptions to the U.S. and global economy and has contributed to significant volatility and negative pressure in financial markets. The global impact of the outbreak is continually evolving and, as additional cases of the virus are identified, many countries, including the U.S., have reacted by instituting quarantines, restrictions on travel and other public health safety measures. Such orders, restrictions and recommendations, and the perception that additional orders, restrictions or recommendations could occur, have resulted in widespread closures of businesses not deemed “essential,” work stoppages, slowdowns and delays, work-from-home policies, travel restrictions and cancellation of events, as well as record declines in stock prices, among other effects. Although some states are starting to relax quarantines and similar restrictions, the regulations vary on a state by state basis and the impact of loosening of those restrictions is not yet known.

The extent to which COVID-19 may impact our preclinical studies or clinical trial operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, the severity of COVID-19, or the effectiveness of actions to contain and treat COVID-19. The continued spread of COVID-19 globally could adversely impact our preclinical studies or clinical trial operations in the United States, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. COVID-19 may also affect employees of third-party CROs located in affected geographies that we rely upon to carry out our clinical trials. Any negative impact COVID-19 has to patient enrollment or treatment or the execution of our current product candidates and any future product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our current product candidate and any future product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

Further, the COVID-19 outbreak may delay enrollment in our clinical trials due to diversion or prioritization of trial site resources away from the conduct of clinical trials and toward the COVID-19 pandemic. Key clinical trial activities, such as site monitoring, may be interrupted due to restrictions in travel, and some patients may be unwilling to enroll in our trials or be unable to comply with clinical trial protocols if quarantines or travel restrictions impede patient movement or interrupt healthcare services, which would delay our ability to conduct clinical trials or release clinical trial results. The spread of COVID-19, or another infectious disease, could also negatively affect the operations at our third-party manufacturers, which could result in delays or disruptions in the supply of our current product candidates and any future product candidates. In addition, we may continue to take temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring all employees to work remotely, suspending all non-essential travel worldwide for our employees, and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business.

Additionally, timely enrollment in our clinical trials is dependent upon clinical trial sites which may be adversely affected by global health matters, such as pandemics. Some factors from the COVID-19 outbreak that may adversely affect enrollment in the clinical trials of our product candidates include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- limitations on travel that could interrupt key trial activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, and delay or inability to secure visas or entry permission, as applicable;
- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and conditioning drugs and other supplies used in our clinical trials; and
- employee disruptions caused by workplace closures, staffing shortages, travel limitations or mass transit disruptions, that could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

We cannot presently predict the scope and severity of any potential business shutdowns or disruptions. If we or any of the third parties with whom we engage were to experience additional shutdowns or other prolonged business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could have a material adverse impact on our business and our results of operation and financial condition.

Risks Related to Development of our Product Candidates

We depend heavily on the success of our product candidates. Even if we obtain favorable clinical results, we may not be able to obtain regulatory approval for, or successfully commercialize any of our product candidates.

We rely on our lead product candidates, and our business depends almost entirely on the successful clinical development, regulatory approval and commercialization of such product candidates, which may never occur. We have experienced setbacks in the development of our product candidates and we are currently evaluating our development options. For example, in January 2021, following the announcement regarding the topline results from the Phase 2 clinical trial of razuprotafib in patients with elevated IOP associated with OAG or OHT, we initiated a process to explore a range of strategic alternatives focused on maximizing stockholder value from our clinical assets and cash resources. While the Phase 2 trial met the primary efficacy endpoint at Day 28 with the BID group, the IOP decrease was not at a level deemed sufficient to move to Phase 3 development.

In addition, in May 2020, we were selected by Quantum Leap Healthcare Collaborative to participate in the I-SPY COVID Trial to evaluate razuprotafib for the treatment of COVID-19 related ARDS in adult patients with critical COVID-19. In September 2020, we announced the first patient was dosed with razuprotafib in the I-SPY COVID-19 trial. The I-SPY COVID trial is an investigator-sponsored clinical trial, which is being conducted by Quantum Leap Healthcare Collaborative. While we have provided input to I-SPY with respect to the razuprotafib arm of the I-SPY COVID clinical trial, we have not controlled and do not control the design or administration of investigator-sponsored clinical trials, nor the submission or approval of any IND or foreign equivalent required to conduct these trials. As a result, investigator-sponsored trials could, depending on the actions of such third parties, jeopardize the validity of the clinical data generated, identify significant concerns with respect to our product candidates that could impact our findings or clinical trials, and adversely affect our ability to obtain marketing approval from the FDA or other applicable regulatory authorities. To the extent the results of this or other investigator-sponsored trials are inconsistent with, or different from, the results of our company-sponsored trials or raise concerns regarding our product candidates, the FDA or a foreign regulatory authority may question the results of the company-sponsored trial, or subject such results to greater scrutiny than it otherwise would. In these circumstances, the FDA or such foreign regulatory authorities may require us to obtain and submit additional clinical data, which could delay clinical development or marketing approval of our product candidates. In addition, while investigator-sponsored trials could be useful to inform our own clinical development efforts, there is no guarantee that we will be able to use the data from these trials to form the basis for regulatory approval of our product candidates.

In January 2021, the Data Monitoring Committee recommended discontinuation of razuprotafib in the I-SPY COVID-19 trial after 21 patients due to the complexity of monitoring patients in the setting of a surge in ICU patients. There were no apparent safety signals associated with razuprotafib in these 21 patients and we believe the scientific basis is sound for continuing to evaluate the drug in patients presenting with ARDS across a broader array of infections.

In August 2020, we announced a second COVID-19 trial to evaluate subcutaneous razuprotafib for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 as part of the MTEC-20-09-COVID-19 Treatment Military Infectious Disease Research Program ("MIDRP") ("RESCUE" trial). The Medical Technology Enterprise Consortium ("MTEC"), a non-profit organization primarily funded by the U.S. Army Medical Research and Development Command, will provide up to $5.1 million of reimbursement related to qualified internal and external spending, as it relates to the clinical trial. In February 2021, we decided to stop recruiting after the first 31 patients were enrolled based on challenges recruiting and monitoring patients in the current pandemic environment. There were no apparent safety signals associated with dosing COVID-19 patients in the RESCUE trial and we plan to further analyze the data to assess trends in efficacy and biomarkers. We expect to report top-line data in the second quarter of 2021.

For both the I-SPY COVID-19 and RESCUE trials, investigation into the therapeutic potential of razuprotafib in this indication is in its early stages and is exploratory, and there can be no assurance that the development of razuprotafib will yield promising results in this indication or that such development will be successful or otherwise proceed on the anticipated timelines or within the anticipated budget.

We currently have no products for sale, generate no revenues from sales of any drugs, and may never be able to develop marketable products. Our product candidates will require substantial additional clinical development, testing, manufacturing process development, and regulatory approval before we are permitted to commence commercialization. We are currently in preclinical development for ARP-1536, which is our other product candidate that we are developing internally. None of our product candidates has advanced into a pivotal trial, and it may be years before such a 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 any of our product candidates.

We are not permitted to market any of our product candidates 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, we must conduct and complete further clinical trials, including Phase 3 clinical trials, and any additional nonclinical studies or clinical trials required by the FDA. To date, we have completed only a limited number of clinical trials with our product candidates. 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. Our development activities could be harmed or delayed by a partial shutdown of the U.S. government, including the FDA. We have not obtained regulatory approval for any product candidate and it is possible that none of our product candidates will ever receive regulatory approval. The FDA may delay, limit or deny approval of our product candidates for many reasons, including, among others:

- we may not be able to demonstrate that our product candidates are safe and effective in any indications that may be pursued for the product candidate, 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 our product candidates;
- the FDA may require that we conduct additional clinical trials;

- the contract research organizations (“CROs”) or the clinical investigators that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;
- we, our CROs or clinical investigators may fail to perform in accordance with the FDA’s good clinical practice (“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 may require 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 our product candidates 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 our product candidates. Because our business is substantially dependent upon our product candidates, 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 (“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 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, and there is no guarantee that we can successfully enroll patients in a timely manner for our clinical trials. 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.

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 razuprotafib or any other product candidate in relation to available therapies or other products under development;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;

- ability to monitor patients adequately during and after treatment; and
- factors we may not be able to control, such as current or potential pandemics that may limit patients, principal investigators or staff or clinical site availability (*e.g.*, the COVID-19 pandemic).

Clinical drug development is a lengthy and expensive process with an uncertain outcome, and positive results from preclinical studies or earlier stage clinical trials are not necessarily predictive of the results of our future clinical trials. If we cannot replicate the positive results from preclinical studies or earlier stage clinical trials in subsequent clinical trials, we may be unable to successfully develop, obtain regulatory approval for and commercialize our product candidates.

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, while our Phase 2 trial met the primary efficacy endpoint at Day 28 with the BID group, the IOP decrease was not at a level deemed sufficient to move to Phase 3 development . There can be no assurance that the results of any clinical trials that we may undertake in the future will produce positive results. In addition, later stage clinical trials are expected to enroll a larger number of subjects and will treat subjects for longer periods than earlier stage 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.

Interim, "topline," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock after this offering.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the interim, topline, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

We may experience delays in the conduct of any clinical trials we may undertake in the future, and we do not know whether such 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 ("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.

In addition, disruptions caused by the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing 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 ("DSMB") for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination, including a clinical hold, 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, unforeseen safety issues or adverse side effects including those experienced by other product candidates in the same class as our product candidates, 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.

Risks Related to Regulatory Review and Approval of Product Candidates

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, establishment registration, as well as continued compliance with current Good Manufacturing Practice ("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.

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.

We may conduct our clinical trials for our product candidates in trial sites outside of the United States, including Japan, the United Kingdom and the European Union, and seek regulatory approval for our product candidates in major markets in addition to the United States, including the European Union, the United Kingdom and Japan. 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 our product candidates 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.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, on March 10, 2020 the FDA announced its intention to postpone most inspections of foreign manufacturing facilities while local, national and international conditions warrant. On March 18, 2020, the FDA announced its intention to temporarily postpone routine surveillance inspections of domestic manufacturing facilities and provided guidance regarding the conduct of clinical trials which the FDA continues to update. As of June 23, 2020, the FDA noted it was conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. On July 10, 2020, the FDA announced its goal of restarting domestic on-site inspections during the week of July 20, 2020, but such activities will depend on data about the virus' trajectory in a given state and locality and the rules and guidelines that are put in place by state and local governments. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

Risks Related to Our Intellectual Property

Risks Related to Protecting 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.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our pending and future patent applications may not result in issued patents that protect our technology or products, in whole or in part. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies. 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. Likewise, a competitor may make and market a product similar to our products but that are not covered by the scope of our patents. 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. In addition, our patents will eventually expire, and the active pharmaceutical ingredients in our current product candidates will become commercially available in generic drug products. Thus, no patent protection may be available with regard to formulation or method of use.

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. Moreover, the inventors of our patents or patent applications or our scientific consultants may become involved with competitors, develop products or processes which design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors. Likewise, our collaborators may become hostile to us or develop products or processes that are adjacent to or compete with us, including products and processes outside the scope of our patents. For example, a hostile collaborator may use technology similar to ours to pursue treatment of an indication that we plan to pursue, and may obtain approval for a product before we do. A hostile collaborator may file patent applications based on information learned from us. Such patent applications may become prior art that will be detrimental to future patent applications by us on similar technology.

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 ("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. We, or our collaborators, might not have been the first to file patent applications on certain inventions. Likewise, our collaborators may file patent applications on certain inventions without our knowledge, prior to our filing patent applications on those inventions. 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, willfully or unintentionally, or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our licensors, collaborators, and suppliers. 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, which we have licensed to Gossamer as part of the June 24, 2018 license agreement. 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. The occurrence of any of the foregoing may negatively impair our collaboration with Gossamer and prevent us from realizing the intended benefits of this collaboration.

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, even if we are successful in stopping infringement of our patents.

There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third party on the ground that such third party’s activities do not infringe our patents. In addition, the U.S. Supreme Court has recently changed some legal principles that affect patent applications, granted patents and assessment of the eligibility or validity of these patents.

As a consequence, issued patents may be found to contain invalid claims according to the newly revised eligibility and validity standards. Some of our patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in proceedings before the USPTO, or during litigation, under the revised criteria which could also make it more difficult to obtain patents.

We may not be able to detect infringement against our patents, as the case may be, which may be especially difficult for formulation patents. Even if we detect infringement by a third party of our patents, we may choose not to pursue litigation against or settlement with the third party. If we later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us to enforce our patents against such third party.

If another party questions the patentability of any of our claims in our U.S. patents, the third party can request that the USPTO review the patent claims such as in an *inter partes* review, *ex parte* re-exam or post-grant review proceedings. These proceedings are expensive and may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings in the European Patent Office ("EPO") or similar proceedings in other foreign patent offices, where our foreign patents are challenged. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business.

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. Moreover, enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful. These lawsuits also may impact our ability to pursue agreements with third parties in the future.

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. A collaborator at such academic institution may use the information learned from the collaboration to compete with us, either in an academic or commercial setting. The collaborator may use the results obtained through the academic collaboration for the benefit of another commercial entity. The collaborator may use technology for the benefit of a third party even if we were entitled to a license or the right to negotiate for a license to the technology from the academic institution. 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.

Moreover, our reliance on third parties may be exploited by a third party with knowledge of our Company, including knowledge of our Company strategies, intellectual property, research programs, trade secrets, and scientific discovery including, for example, drug targets, pharmaceutically active ingredients, dosing regimens and mechanisms of action. A third party may start a competing company or may join a competing company. If a third party with whom we have an agreement does become a competitor, this may lead to questions of intellectual property ownership, ownership of physical assets, inventorship and breach of contracts in place with the third party. If we seek to resolve this issue by a lawsuit, then we expect counter claims that may jeopardize the validity and enforceability of our patents. The third parties with whom we collaborate also may have business or legal conflicts of interest. These conflicts of interest can lead to litigation or impact the ability of the third party to fulfill their obligations to us.

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 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 Intellectual Property Litigation

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 razuprotafib 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, then 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, then 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 acquire or obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and there can be no assurance that we will be able to do so on commercially reasonable terms or at all.

Additionally, we may in the future from time to time collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program. The institution also may only offer a nonexclusive license, providing an opportunity for competitors to license intellectual property important to us. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of such program and our business and financial condition could suffer. The academic institutions, or our collaborators at those institutions, also may violate the terms of our agreements with them. For example, a collaborator could use proprietary knowledge based on the collaboration to compete with us. These violations may result in litigation, which can be costly and may impact our ability to use resources for product development or other necessary functions.

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

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.

Risks Related to Our Business and Industry

Risks Related to Our Employee Matters

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

We are highly dependent on members of our senior management and loss of the services of any of these persons could impede the achievement of our objectives, including with respect to our efforts for the exploration of strategic alternatives.

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. In addition, in January 2021, we adopted a realignment plan to reduce operating costs and better align our workforce with the needs of our ongoing business. The realignment plan reduced our workforce by 7 employees, representing approximately 58% of our workforce. As a result, while we have undertaken efforts to retain our current employees, we may experience challenges in doing so.

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 conduct our business 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, 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 if 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 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.

Risks Related to Our Business Operations and Growth

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 Our Reliance on Third Parties

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.

We are currently exploring our development options for our product candidates, and such options may include strategic collaborations and licenses for the future development of our assets. 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.

On June 24, 2018, we entered into a license agreement with Gossamer (the "Gossamer License Agreement") pursuant to which we granted to Gossamer an exclusive, sublicensable license to develop and commercialize AKB-4924 and other structurally related products worldwide. We received an upfront payment of $20.0 million in connection with the Gossamer License Agreement and are eligible to receive additional payments contingent upon the achievement of specified milestones. On May 12, 2020, we entered into that certain Amendment No. 1 to the Gossamer License Agreement ("Amendment No. 1" and together with the Gossamer License Agreement, as amended by Amendment No. 1, the "Amended Gossamer License Agreement") and received a payment of $15.0 million in conjunction with the terms of the Amendment 1. We are also eligible to receive tiered royalties on sales of licensed products and additional payments upon the occurrence of specified events involving the licensed products. However, there can be no assurance that we will satisfy the conditions to receive any such payments from Gossamer in a timely manner or at all. While Gossamer is obligated to use its commercially reasonable efforts to develop and commercialize the licensed products, there can be no assurance that such products would be successfully developed and commercialized. In addition, the Amended Gossamer License Agreement contains an exclusivity provision pursuant to which we are prohibited from developing, manufacturing or commercializing certain HIF stabilizing compounds as described in the agreement. While the license agreement expires on a licensed product-by-licensed product and country-by-country basis on the later of fifteen years from the date or first commercial sale or when there is no longer a valid patent claim covering such licensed product in such country, either party may terminate the Amended Gossamer License Agreement for an uncured material breach by the other party or upon the bankruptcy or insolvency of the other party. In addition, Gossamer may terminate the Amended Gossamer License Agreement in the event it determines that there is a potential safety or efficacy issue with the licensed products. Therefore, there can be no assurance that the Amended Gossamer License Agreement will continue for its full duration or that we will realize the intended benefits.

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 Financial Position and Need for Additional Capital

Risks Related to Past Financial Condition

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 two product candidates that we are developing internally, 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.

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 and comprehensive losses each year since our inception, with the exception of the three months ended September 30, 2018 and June 30, 2020, as a result of the upfront Gossamer payments discussed above. For the year ended December 31, 2020 and 2019, we incurred net and comprehensive loss of $4.3 million and $23.3 million, respectively. As of December 31, 2020, we had an accumulated deficit of $146.6 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 plans for development of our product candidates and our ability to obtain funding through equity or debt financings, strategic collaborations or grants to fund such development.

We expect to continue to incur significant expenses and operating losses for the foreseeable future, including to sustain our operations while we evaluate our development options for our product candidates, seek strategic alternatives and to operate as a public reporting 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 (“FDA”) the European Medicines Agency (“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 and comprehensive income (loss) 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.

Our corporate restructuring and the associated headcount reduction may not result in anticipated savings, could result in total costs and expenses that are greater than expected and could disrupt our business.

In January 2021, we initiated a realignment plan to reduce operating costs and better align its workforce with the needs of our ongoing business. The realignment plan, reduces its current workforce by 7 employees, representing approximately 58% of our workforce. As a result of this realignment plan, we estimate we will incur one-time employee related severance expenses of approximately $1.2 million in the first quarter of 2021. We anticipate the majority of the one-time employee severance liability to be paid during 2021. We may not realize, in full or in part, the anticipated benefits, savings and improvements in our cost structure from our restructuring efforts due to unforeseen difficulties, delays or unexpected costs. If we are unable to realize the expected operational efficiencies and cost savings from the restructuring, our operating results and financial condition would be adversely affected. Furthermore, our restructuring plan may be disruptive to our operations. For example, our headcount reductions could yield unanticipated consequences, such as increased difficulties in implementing our business strategy, including retention of our remaining employees.

Risks Related to Future Financial Condition

We do not have any committed sources of outside capital. A failure to obtain necessary capital when needed to sustain our business could force us to suspend our operations.

As of December 31, 2020, our cash and cash equivalents were $42.6 million. We are currently evaluating our development options for our product candidates. Any efforts for continued program development will be time-consuming and expensive.

Based on our current operating plan, and absent any future financings or strategic partnerships, we believe that our existing cash and cash equivalents will be sufficient to fund our projected operating expenses and capital expenditure requirements through the fourth quarter of 2022. 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. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact our ability to access capital as and when needed. If adequate funds are not available to us on a timely basis, we may be required to suspend our operations.

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.

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. For example, in June 2018, we entered into a license agreement with Gossamer for the development and commercialization of AKB-4924.

If we are unable to raise additional funds through equity or debt financing when needed, we may be required to suspend our operations.

Risks Related to Commercialization

Risks Related to Sales, Marketing and Competition

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 one or more of our product candidates, 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.

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.

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.

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. 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.

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;
- state and federal transparency reporting requirements that require us to register our sales representatives and report any gifts, payments for speaking engagements, travel costs, donations, or other support offered to physicians or teaching hospitals which may create additional burden on sales and marketing personnel;
- our inability to effectively manage a 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.

Our product candidates 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 product candidates 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. 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 trials evaluating the safety and tolerability of subcutaneous razuprotafib have been dizziness and asymptomatic decreases in blood pressure, and these adverse events may occur in future development by this route of administration. The most common adverse event seen in the Phase 1b and Phase 2 clinical trials evaluating the safety and tolerability of topical ocular razuprotafib was mild conjunctival hyperemia. Our understanding of the relationship between razuprotafib 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.

With respect to the potential use of razuprotafib for the treatment of ARDS associated with COVID-19, clinical development remains in the early stages. As a result, while we believe razuprotafib may have a favorable tolerability profile in this patient population, there can be no assurance that we will not observe the incidence of adverse events or serious adverse events upon further development of razuprotafib. For example, the incidence of adverse events and serious adverse events may be magnified in this patient population due to the critical and often life-threatening nature of the underlying disease.

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 Healthcare Regulation

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.

Our future revenues and profitability will be adversely affected if United States and foreign governmental, private third-party insurers and payors and other third-party payors, including Medicare and Medicaid, do not agree to defray or reimburse the cost of our products to the patients. If these entities fail to provide coverage and reimbursement with respect to our products or provide an insufficient level of coverage and reimbursement, our products may be too costly for some patients to afford them and physicians may not prescribe them. 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. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicate determinations. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. 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. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our product candidates even if there is adequate coverage and reimbursement from third party payors.

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

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, actions and proposals to control and reduce healthcare costs. There have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any of our products or product candidates for which we obtain marketing approval.

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 Affordable Care Act ("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% (increased to 70% as of January 1, 2019 pursuant to subsequent legislation) 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. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, and the 2020 Omnibus Bill, these reductions are suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. As the legislation currently stands, the reductions will go back into effect April 2021 and will remain in effect through 2030 unless additional Congressional action is taken.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. Various portions of the ACA are currently undergoing legal and constitutional challenges in the United States Supreme Court; the Trump Administration had issued various Executive Orders which eliminated cost sharing subsidies and various provisions 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; and Congress has introduced several pieces of legislation aimed at significantly revising or repealing the ACA. The United States Supreme Court is expected to rule on a legal challenge to the constitutionality of the ACA in early 2021. As implementation of the ACA is ongoing, the law appears likely to continue the downward pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs. Litigation and legislation related to the ACA are likely to continue, with unpredictable and uncertain results. We will continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

Moreover, the Drug Supply Chain Security Act imposed new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be.

The Trump administration released a plan to lower drug prices and reduce out of pocket costs of drugs that contained proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. On July 24, 2020 and September 13, 2020, President Trump announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. The FDA also released a final rule on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada.

On November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. The Interim Final Rule has not been finalized and is subject to revision and challenge. Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers.

Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse, revoke, or otherwise change these measures, Congress has indicated that it will continue to seek new legislative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. It is unclear what effect such changes will have on our business and our ability to receive adequate reimbursement for our future products. Some of these proposed measures, including drug importation and pharmacy benefit manager rebate rule changes, face legal challenges from industry groups and participants. We cannot predict whether additional reform initiatives may be adopted in the future or whether initiatives that have been adopted will be repealed or modified, or whether legal challenges will be successful. 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 expect that changes and challenges to the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies, and additional downward pressure on the price that we receive for any future approved product.

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.

Healthcare providers, physicians and third-party payors in the United States and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, which may constrain the business or financial arrangements and relationships through which such companies sell, market and distribute pharmaceutical products. In particular, the promotion, sales and marketing of healthcare items and services, as well as a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. The applicable federal and state healthcare laws and regulations laws that may affect our ability to operate include, but are not limited to:

- The federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, overtly or covertly, in cash or in kind, 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. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, they are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties statute. Violations of the AKS carry potentially significant civil and criminal penalties, including imprisonment, fines, administrative civil monetary penalties, and exclusion from participation in federal healthcare programs.

- The federal anti-inducement law which prohibits, among other things, the offering or giving of remuneration, which includes, without limitation, any transfer of items or services for free or for less than fair market value (with limited exceptions), to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a federal or state governmental program.
- Federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, or the FCA, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used, a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Companies that submit claims directly to payors may also be liable under the FCA for the direct submission of such claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery. When an entity is determined to have violated the federal civil False Claims Act, the government may impose civil fines and penalties for each false claim, plus treble damages, and exclude the entity from participation in Medicare, Medicaid and other federal healthcare programs.
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, and its implementing regulations, which prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses, otherwise known as covered entities, relating to the privacy, security and transmission of individually identifiable health information, including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.
- The federal transparency requirements under the Affordable Care Act, including the Physician Payment Sunshine Act, which require drug and biologics manufacturers eligible for payment under Medicare, Medicaid or the Children's Health Insurance Program to report annually to HHS, information related to payments or other "transfers of value" made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners.

- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.
- State and foreign 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 scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies continue to give regular and close scrutiny to interactions between healthcare companies, including pharmaceutical manufacturers, and healthcare providers, and such scrutiny often leads to investigations, prosecutions, convictions and settlements in the healthcare industry. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

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 administrative, 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. Any action for violation of these laws, even if successfully defended, could cause a pharmaceutical manufacturer to incur significant legal expenses and divert management's attention from the operation of the business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect business in an adverse way.

Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct 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.

In addition, the approval and commercialization of any of our products outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Risks Related to Ownership of Our Common Stock

Risks Related to Investments in Our Securities

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.

The market price of our common stock is likely to be volatile. Since our common stock became listed on Nasdaq Capital Market on June 26, 2018, the trading price of our common stock has ranged from $0.42 to $4.35 per share. The market price of our common stock may continue to 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 may continue to 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.

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 ("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 regarding 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 consolidated 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 following the date of completion of our initial public offering, 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 $250 million as of June 30 in any given year (or $700 million if we had less than $100 million in revenues), 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.

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

The Financial Industry Regulatory Authority ("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.

If we are unable to maintain compliance with Nasdaq Capital Market listing standards, including maintenance of at least $2.5 million of stockholders' equity and maintenance of a $1.00 minimum bid price, our common stock may be delisted from the Nasdaq Capital Market and you may face significant restrictions on the resale of your shares due to state "blue sky" laws.

There can be no assurances that we will be able to maintain our Nasdaq Capital Market listing in the future. On July 24, 2019, we were notified by Nasdaq Stock Market, LLC ("Nasdaq") that we were not in compliance with the minimum bid price requirements set forth in Nasdaq Listing Rule 5550(a)(2) for continued listing on the Nasdaq Capital Market. Nasdaq Listing Rule 5550(a)(2) requires listed securities to maintain a minimum bid price of $1.00 per share and Nasdaq Listing Rule 5810(c)(3)(A) provides that a failure to meet the minimum bid price requirement exists if the deficiency continues for a period of 30 consecutive business days. To regain compliance, the bid price of our common stock must have a closing bid price of at least $1.00 per share for a minimum of 10 consecutive business days. In June 2020, we were notified by Nasdaq that the closing bid price of our common stock was maintained for a minimum of 10 consecutive business days and, therefore, we regained compliance with the minimum bid price requirement. However, there can be no assurance that we will not encounter challenges with maintaining compliance with Nasdaq Capital Market listing standards in the future.

In the event we are unable to maintain compliance with the Nasdaq Capital Market listing standards and our common stock is delisted from the Nasdaq Capital Market, it would, among other things, likely lead to a number of negative implications, including an adverse effect on the price of our common stock, reduced liquidity in our common stock, the loss of federal preemption of state securities laws and greater difficulty in obtaining financing. In the event of a de-listing, we would take actions to restore our compliance with Nasdaq's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq Capital Market minimum bid price requirement in the future, or prevent future non-compliance with Nasdaq's listing requirements. If we cannot restore our compliance with Nasdaq's listing requirements, we would pursue eligibility for trading of these securities on other markets or exchanges, such as the OTCQB or OTCQX, which are unorganized, inter-dealer, over-the-counter markets which provides significantly less liquidity than the Nasdaq Capital Market or other national securities exchanges.

Furthermore, each state has its own securities laws, often called "blue sky" laws, which (1) limit sales of securities to a state's residents unless the securities are registered in that state or qualify for an exemption from registration, and (2) govern the reporting requirements for broker-dealers doing business directly or indirectly in the state. Before a security is sold in a state, there must be a registration in place to cover the transaction, or it must be exempt from registration. The applicable broker-dealer must also be registered in that state. If we fail to maintain our Nasdaq Capital Market listing, then we may not be considered to be on a national exchange and do not know whether our securities will be registered or exempt from registration under the laws of any state.

A determination regarding registration will be made by those broker-dealers, if any, who agree to serve as market makers for our common stock. There may be significant state blue sky law restrictions on the ability of investors to sell, and on purchasers to buy, our securities. You should therefore consider the resale market for our common stock to be limited, as you may be unable to resell your shares without the significant expense of state registration or qualification.

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, 2020, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 27.65% 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 only recently became listed on a national securities exchange, we may obtain research coverage from fewer analysts than we would have obtained. 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 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 could 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 and an additional registration statement covering 9,497,337 shares purchased by certain stockholders in June 2018 and subsequent open market purchases. 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 preserve our cash resources during our efforts to explore strategic alternatives for our company. Although we currently intend to use our cash and cash equivalents in such a manner, we will have broad discretion in the application of such cash and cash equivalents. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or loses value.

As a result of 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 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 we are not able to demonstrate compliance with the Sarbanes-Oxley Act, our internal control over financial reporting is perceived as inadequate, or 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 maintain our 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 consolidated 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 following this annual report until 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.

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.

An active trading market for our common stock may not develop or be sustainable. If an active trading market does not develop, investors may not be able to resell their shares at or above the purchase price and our ability to raise capital in the future may be impaired.

Our common stock has been listed on The Nasdaq Capital Market since June 26, 2018. The initial listing price for our common stock was determined through negotiations with the underwriters. This price may not reflect the price at which investors in the market will be willing to buy and sell our shares. Although our common stock is listed on The Nasdaq Capital Market, an active trading market for our shares may never develop or, if developed, be maintained. If an active market for our common stock does not develop or is not maintained, it may be difficult for you to sell shares you purchase without depressing the market price for the shares or at all. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.

The global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. We believe that the state of global economic conditions are particularly volatile and uncertain, not only in light of the COVID-19 pandemic and the potential global recession resulting therefrom, but also due to recent and expected shifts in political, legislative and regulatory conditions concerning, among other matters, international trade and taxation, and that an uneven recovery or a renewed global downturn may negatively impact our ability to conduct clinical trials on the scale and timelines anticipated. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business or political environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make obtaining any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our operating goals on schedule and on budget. To the extent that our profitability and strategies are negatively affected by downturns or volatility in general economic conditions, our business and results of operations may be materially adversely affected.

Risks Related to Our Charter and Bylaws

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.

Risks Related to Tax

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 (the “Code”) a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating losses (“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 as no studies have been performed to evaluate a change in ownership. 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.

General Risk Factors

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

Our business and operations would suffer if we sustain cyber-attacks or other privacy or data security incidents that result in security breaches.

Our information technology may be subject to cyber-attacks, security breaches or computer hacking. Experienced computer programmers and hackers may be able to penetrate our security controls and misappropriate or compromise sensitive personal, proprietary or confidential information, create system disruptions or cause shutdowns. They also may be able to develop and deploy malicious software programs that attack our systems or otherwise exploit any security vulnerabilities. Our systems and the data stored on those systems may also be vulnerable to security incidents or security attacks, acts of vandalism or theft, misplaced or lost data, human errors, or other similar events that could negatively affect our systems and our data, as well as the data of our business partners. Further, third parties that provide services to us, could also be a source of security risk in the event of a failure of their own security systems and infrastructure.

The costs to eliminate or address the foregoing security threats and vulnerabilities before or after a cyber-incident could be significant. Our remediation efforts may not be successful and could result in interruptions, delays or cessation of service, and loss of existing or potential suppliers, manufacturers or other third parties. In addition, breaches of our security measures and the unauthorized dissemination of sensitive personal, proprietary or confidential information about us, our business partners, participants in our clinical trials or other third parties could expose us to significant potential liability and reputational harm. In addition, the loss of clinical trial data from completed or ongoing or planned clinical trials as a result of a data security incident or other systems failure could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. As threats related to cyber-attacks develop and grow, we may also find it necessary to make additional investments to protect our data and infrastructure, which may impact our profitability. We could also be negatively impacted by existing and proposed laws and regulations, as well as government policies and practices related to cybersecurity, data privacy, data localization and data protection such as GDPR.

Our business and operations may be negatively impacted by the United Kingdom's withdrawal from the European Union.

On June 23, 2016, the United Kingdom held a referendum in which a majority of the eligible members of the electorate voted to leave the European Union, commonly referred to as Brexit. Pursuant to Article 50 of the Treaty on European Union, the United Kingdom ceased being a Member State of the European Union on January 31, 2020. There was a transitional period, during which European Union's rules continued to apply in the United Kingdom, however this ended on December 31, 2020. The United Kingdom and European Union have signed a EU-UK Trade and Cooperation Agreement, which became provisionally applicable on January 1, 2021 and will become formally applicable once ratified by both the United Kingdom and the European Union. This agreement provides details on how some aspects of the United Kingdom and European Union's relationship regarding medicinal products will operate, particularly in relation to Good Manufacturing Practice, however there are still many uncertainties. Many of the regulations that now apply in the United Kingdom following the transition period (including financial laws and regulations, tax, intellectual property rights, data protection laws, supply chain logistics, environmental, health and safety laws and regulations, medicine approval and regulations, immigration laws and employment laws), will likely be amended in future as the United Kingdom determines its new approach, which may result in significant divergence from European Union regulations. This lack of clarity on future United Kingdom laws and regulations and their interaction with the European Union laws and regulations increases our regulatory burden of operating in and doing business with both the United Kingdom and the European Union.

The long-term effects of Brexit will depend in part on how the EU-UK Trade and Cooperation Agreement, and any future agreements signed by the United Kingdom and the European Union, take effect in practice. Such a withdrawal from the European Union is unprecedented, and it is unclear how the restrictions on the United Kingdom's access to the European single market for goods, capital, services and labor and the wider commercial, legal and regulatory environment, could impact our current and future operations and clinical activities in the United Kingdom.

We may also face new regulatory costs and challenges that could have an adverse effect on our operations as a result of Brexit. The United Kingdom will lose the benefits of global trade agreements negotiated by the European Union on behalf of its members, which may result in increased trade barriers that could make our doing business in the European Union or European Economic Area more difficult. We expect that, now the transition period has expired, Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which European Union laws to replicate or replace, including those related to the regulation of medicinal products. Any of these effects of Brexit, and others we cannot anticipate, could negatively impact our business and results of operations in the United Kingdom.

The uncertainty concerning the United Kingdom's legal, political and economic relationship with the European Union following Brexit may also be a source of instability in the international markets, create significant currency fluctuations, and/or otherwise adversely affect trading agreements or similar cross-border co-operation arrangements (whether economic, tax, fiscal, legal, regulatory or otherwise).

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters consist of 7,580 square feet of leased office space in Cincinnati, Ohio. Our lease expires on July 31, 2021.

We believe our existing facility is 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

Our common stock began trading on the OTC Markets – OTCQB Tier on August 8, 2017 and subsequently uplisted to the Nasdaq Capital Market on June 26, 2018 under the symbol “ARPO.” The following table sets forth, for the periods indicated, the high and low intraday sales prices of our common stock as reported by the Nasdaq Capital Market and OTC Markets – OTCQB Tier.

	Common Stock	
	High	Low
2020		
First Quarter	$ 0.71	$ 0.42
Second Quarter	$ 1.53	$ 0.49
Third Quarter	$ 1.90	$ 1.04
Fourth Quarter	$ 2.31	$ 0.96
	High	Low
2019		
First Quarter	$ 4.25	$ 0.88
Second Quarter	$ 1.16	$ 0.85
Third Quarter	$ 0.90	$ 0.61
Fourth Quarter	$ 0.70	$ 0.45

Stockholders

As of March 8, 2021, there were 113 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.

Issuer Purchases of Equity Securities

There were no repurchases of shares of common stock made during the year ended December 31, 2020.

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 consolidated financial statements and the notes to those statements included in this Annual Report on Form 10-K for the year ending December 31, 2020. 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. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report on Form 10-K our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. Please also refer to the section under the heading "Note Regarding Forward-Looking Statements."

Operating Overview

Aerpio Pharmaceuticals, Inc. is a biopharmaceutical company focused on developing compounds that activate Tie2 as well as other indications in which the Company believes that activation of Tie2 may have therapeutic potential. Our product candidates include razuprotafib (formerly known as AKB-9778), a small molecule VE-PTP inhibitor.

In March 2019, we announced topline results from our Phase 2b ("TIME-2b") clinical trial of AKB-9778 for the treatment of non-proliferative diabetic retinopathy. Although the results did not meet the study's primary endpoint, we believe that the TIME-2b study further supported the reduction of intraocular pressure ("IOP") seen with subcutaneous razuprotafib in the previous TIME-2 study. Based on these findings, we developed a topical ocular formulation of razuprotafib, and observed in preclinical studies activation of Tie2 in Schlemm's canal, IOP reduction via enhanced outflow facility and favorable tolerability.

In June 2019, we initiated a double-masked, multiple-ascending dose Phase 1b clinical trial for open angle glaucoma ("OAG"). We enrolled four cohorts of 12 subjects each and subjects received increasing daily doses of a topical ocular formulation of razuprotafib or placebo for seven days. The primary endpoint of the trial was ocular safety and tolerability, with IOP lowering as the key pharmacodynamic endpoint. In October 2019, we announced interim results from our Phase 1b clinical trial. The unmasked interim analysis, limited to the first three cohorts, showed the topical ocular administration of razuprotafib was well tolerated. Compared to placebo, there was a dose dependent increase in minimal to mild conjunctival hyperemia with razuprotafib, which was transient and generally considered non-adverse, and a time and dose dependent reduction in IOP that, in the highest once daily ("QD") dose cohort peaked at 4 hours post-dose and was sustained through eight hours on day 7, returning to baseline levels at 24 hours post-dose. Based on these data, a cohort of 43 patients with ocular hypertension ("OHT")/OAG (hypertensive eyes) was added to the ongoing study to assess safety and pilot efficacy in the target patient population.

In January 2020, we announced the results of the fifth cohort of subjects noting subjects in cohort five randomized to the active arm exhibited statistically significant decreases in IOP at all post razuprotafib administration time points on both days 1 and 7 compared with day -1 baseline values when they were being treated with prostaglandin alone. When the change is placebo-corrected, razuprotafib plus prostaglandin versus prostaglandin alone produced a statistically significant decrease in IOP on Day 7 at 0, 4 and 8 hours post dose as compared to placebo. We believe these results suggest a persistent IOP-lowering activity from adding razuprotafib to standard-of-care prostaglandin therapy. Topical ocular administration of razuprotafib was well tolerated over seven days in cohort five. There were no reports of conjunctival hemorrhage or pain on instillation during the seven days of dosing and no systemic/non-ocular AEs were observed.

Based on the preclinical proof of concept and the results of the Phase 1b trial showing a reduction in IOP in patients with OHT and OAG, we initiated a Phase 2 clinical trial in June 2020 designed to evaluate the safety and efficacy of a topical formulation of razuprotafib in approximately 195 patients followed over a 28-day period. Patients enrolled in the trial will be administered a baseline of latanoprost ophthalmic solution 0.005%, and then randomized in a 1:1:1 fashion to receive adjunctive therapy consisting of placebo, 40 mg/ml razuprotafib once-daily, or 40 mg/ml razuprotafib twice-daily. The primary endpoint of the study is mean diurnal IOP at 28 days in the razuprotafib treated groups compared to the latanoprost monotherapy group

In December 2020, we reported that razuprotafib met the primary efficacy endpoint at Day 28 with the twice-daily (“BID”) dose group in our double-blind, placebo-controlled Phase 2 trial in patients with elevated IOP associated with OAG or OHT. The change from baseline in diurnal mean IOP at Day 28 of study eyes treated with razuprotafib BID plus latanoprost showed a statistically significant improvement, or drop in IOP, (two-sided p-value 0.0130 and LS mean difference of -0.92 mm Hg) compared to those treated with latanoprost monotherapy. The razuprotafib once-daily (“QD”) dose group did not show a statistically significant improvement at Day 28. Further analysis of the results demonstrated that razuprotafib had a larger IOP reduction after longer duration dosing (28 days versus 14 days) consistent with its potential mechanism of repairing Schlemm’s canal. Razuprotafib also produced larger IOP reductions in patients with higher starting IOP, or a 1.6 mmHg IOP reduction in patients with post wash-out IOP’s of >26 mmHg and the topical drops were well tolerated in this trial. While the trial met the primary efficacy endpoint at Day 28 with the BID group, the IOP decrease was not at a level deemed sufficient to move to Phase 3 development. Therefore, following the announcement regarding the topline results from the Phase 2 clinical trial of razuprotafib in patients with elevated IOP associated with OAG or OHT, we initiated a process to explore a range of strategic alternatives focused on maximizing stockholder value from our clinical assets and cash resources. As part of this process, we are exploring strategic options for partnering our programs, as well as the potential for an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. There can be no assurance that this exploration of strategic alternatives will result in the Company entering or completing any transaction.

Ladenburg Thalmann & Co. Inc. and Duane Nash, M.D., J.D., M.B.A, have been retained with respect to the strategic review process.

In January 2021, we executed a realignment plan to reduce operating costs and better align our workforce with the needs of our ongoing business. The realignment plan reduces our current workforce by 7 employees, representing approximately 58% of our workforce. As a result of this realignment plan, we estimate that we will incur one-time employee related severance expenses of approximately $1.2 million in the first quarter of 2021. We anticipate the majority of the one-time employee severance liability to be paid during 2021. The charges that we expect to incur in connection with the realignment plan are subject to a number of assumptions, and actual results may differ from our original estimate. We may also incur additional costs not currently contemplated due to events that may occur as a result of, or that are associated with, the realignment plan.

Acute Respiratory Distress Syndrome

Based on results in preclinical studies and observations in patients in TIME-2 and TIME-2b trials, we believe that a vascular endothelial receptor, Tie2, may play a pivotal role in the defense against microvascular breach in ARDS. We hypothesize that razuprotafib, our lead Tie2 activator, may have therapeutic potential for the treatment of COVID-19 associated ARDS and initiated two Phase 2 trials during 2020.

In May 2020, we were selected by Quantum Leap Healthcare Collaborative to participate in the I-SPY COVID Trial (Investigation of Serial studies to Predict Your COVID Therapeutic Response with biomarker Integration and Adaptive Learning) to evaluate subcutaneous razuprotafib for the treatment of COVID-19 related ARDS in adult patients with critical COVID-19 (ClinicalTrials.gov Identifier: NCT04488081). The trial was initiated during the third quarter of 2020 but in January 2021, the Data Monitoring Committee recommended discontinuation of razuprotafib after 21 patients due to the complexity of monitoring patients in the setting of a surge in ICU patients. There were no apparent safety signals associated with razuprotafib in these 21 patients and we believe the scientific basis is sound for continuing to evaluate the drug in patients presenting with ARDS across a broader array of infections.

In August 2020, we announced the receipt of funding to evaluate subcutaneous razuprotafib in a new randomized, investigational trial for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 (“RESCUE” trial; ClinicalTrials.gov Identifier: NCT04511650). The RESCUE trial will evaluate subcutaneous razuprotafib for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 as part of the MTEC-20-09-COVID-19 Treatment Military Infectious Disease Research Program (“MIDRP”). The Medical Technology Enterprise Consortium (“MTEC”), a non-profit organization primarily funded by the U.S. Army Medical Research and Development Command, will provide up to $5.1 million of reimbursement related to qualified internal and external spending of the Company, as it relates to the clinical trial. The RESCUE clinical trial was initiated during the third quarter of 2020 but we decided to stop recruiting in February 2021 after the first 31 patients were enrolled based on challenges recruiting and monitoring patients in the current pandemic environment.

There were no apparent safety signals associated with dosing COVID-19 patients in the RESCUE trial and we plan to further analyze the data to assess trends in efficacy and biomarkers. We expect to report top-line data in the second quarter of 2021.

Diabetic Kidney Disease

In two consecutive trials, TIME-2 and TIME-2b, subcutaneous razuprotafib showed reduction in Urine Albumin-Creatinine Ratio ("UACR"), a measure of progression of diabetic kidney disease. In a post-hoc analysis of the earlier TIME-2 clinical trial, there was a 21% reduction (geometric mean) in UACR from baseline in the razuprotafib treatment arms, but an overall increase in UACR in the placebo arm. The prospective UACR analyses from the recently completed TIME-2b trial largely replicated the results from the previous trial and reinforced the potential beneficial effects of Tie2 activation in diabetic kidney disease. We believe that systemic treatment with razuprotafib 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.

ARP-1536 and Bi-specific Antibody

ARP-1536, our humanized monoclonal antibody directed at the same target as subcutaneous razuprotafib, is in preclinical development. We are evaluating development options for ARP-1536, including subcutaneous injection for the treatment of diabetic vascular complications, e.g., diabetic nephropathy and intravitreal injection as an adjunctive therapy for diabetic macular edema. We are also developing a bispecific antibody that binds both vascular endothelial growth factor ("VEGF") and vascular endothelial protein tyrosine phosphatase ("VE-PTP") which is designed to inhibit VEGF activation and activate Tie2. We believe this bispecific antibody has the potential to be an improved treatment for wet AMD and diabetic macular edema via intravitreal injection.

Gossamer License Agreement

In June 2018, we licensed AKB-4924, a selective stabilizer of hypoxia-inducible factor-1 alpha ("HIF-1 alpha") to Gossamer Bio, Inc. ("Gossamer") AKB-4924, (now called GB004), is being developed for the treatment of inflammatory bowel disease ("IBD"). HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. Gossamer has completed the Phase 1 multiple ascending dose ("MAD") clinical study and is currently running a Phase 1b clinical study in ulcerative colitis ("UC") patients. Gossamer has progressed GB004 during 2019 by completing the Phase 1 trial in healthy volunteers and initiating a Phase 1b study in ulcerative colitis patients of 28-day duration. Gossamer reported topline results from the Phase 1b study in the second quarter of 2020 and announced that, subject to developments in the ongoing COVID-19 pandemic, it initiated a 12-week Phase 2 study of GB004 in patients with mild-to-moderate UC in the second half of 2020. Gossamer is responsible for all remaining development and commercial activities for GB004.

Our primary source of liquidity to date has been through public and private sales of our common stock, redeemable convertible preferred stock, convertible debt and the proceeds from a license agreement entered into with Gossamer (the "Gossamer License Agreement"), as amended by that certain Amendment No. 1 to the Gossamer License Agreement ("Amendment No. 1" and together with the Gossamer License Agreement, as amended by Amendment No. 1, the "Amended Gossamer License Agreement"). For the year ended December 31, 2020, we generated $15.0 million in revenue pursuant to Amendment No. 1.

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 as a result of our ongoing activities. 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.

Except for the Amended Gossamer License Agreement that we entered into with Gossamer in June 2018 and amended in May 2020, 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. There can be no assurance of future revenues either from future payments related to the Amended Gossamer License Agreement, transition services or from our product candidates. 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, 2020, we had an accumulated deficit of $146.6 million and anticipate incurring additional losses for the next several years.

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 $42.6 million at December 31, 2020 and financial condition as of this Annual Report on Form 10-K, we believe our existing cash and cash equivalent will be sufficient to fund currently planned operations through the fourth quarter of 2022. The Company is currently evaluating a range of strategic alternatives focused on maximizing stockholder value from our clinical assets and cash resources. As part of this process, we are exploring strategic options for partnering our programs, as well as the potential for an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. There can be no assurance that this exploration of strategic alternatives will result in the Company entering or completing any transaction.

COVID-19 Considerations:

On March 11, 2020, the World Health Organization declared the outbreak of COVID-19, as a global pandemic, which continues to spread throughout the United States and around the world. The COVID-19 pandemic is evolving, and to date has led to the implementation of various responses, including government-imposed quarantines, stay-at-home orders, travel restrictions, mandated business closures and other public health safety measures. In addition, in response to the spread of COVID-19, we have continued to keep our executive offices closed with our employees continue to work outside of our offices. We are closely monitoring the impact of COVID-19 on all aspects of our business, including how it may impact our planned Phase 2 clinical trial for our glaucoma program, expected timelines and costs on an ongoing basis. We do not yet know the full extent of potential delays or the impact on our business, our planned clinical trial, our research programs, healthcare systems or the global economy and we cannot presently predict the scope and severity of any potential business shutdowns or disruptions. The extent to which COVID-19 ultimately impacts our business, results of operations and financial condition will depend on future developments, which remain highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, new information that may emerge concerning the severity of COVID-19 or the effectiveness of actions to contain COVID-19 or treat its impact, among others. While some states and jurisdictions have started to rollback stay-at-home orders, quarantines and similar restrictions and reopened in phases, the regulations vary on a state by state basis and the impact of loosening of those restrictions is not yet known. If we or any of the third parties with whom we engage were to experience additional shutdowns or other prolonged business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could have a material adverse impact on our business, results of operation and financial condition. In addition, a recurrence of COVID-19 cases could cause other widespread or more severe impacts depending on where infection rates are highest. We continue to monitor developments as we deal with the disruptions and uncertainties relating to the COVID-19 pandemic.

Basis of Presentation

The following discussion highlights our 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 our consolidated financial statements contained in this Annual Report on Form 10-K, which we have prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP" or "GAAP"). You should read the discussion and analysis together with such consolidated financial statements and the related notes thereto.

Components of Consolidated Statements of Operations and Comprehensive Loss

License Revenue, and Other

License revenue relates to the Gossamer License Agreement.

Research and Development Expenses

Research and development expenses are expensed as incurred. Research and development expenses consist primarily 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 ("CRO's") and consultants, (iii) the cost of acquiring, developing, and manufacturing clinical study materials, and (iv) costs associated with preclinical, clinical and regulatory activities.

Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and clinical sites.

General and Administrative Expenses

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

Restructuring Expense

Restructuring expense consists primarily of severance related expenses of employees terminated as a result of our restructuring efforts. Expenses include continued payroll, benefits and outplacement services (collectively "severance") as defined and agreed upon by the respective employees' severance agreement. Severance is recognized as restructuring expense when employees are notified of the restructuring event with a corresponding restructuring accrual which was reduced as payments are made to the employees.

Other Income

Other income represents reimbursed internal and external qualified expenses, per the terms of the MTEC arrangement, related to the ARDS RESCUE clinical trial. Other income is recorded, and generally received, in the period the internal or external qualified clinical trial as we incur and pay expenses.

Grant Income

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

Interest Income

Interest income consists of interest income received on cash and cash equivalents.

Results of Consolidated Operations

The following tables set forth our results of operations:

	Years Ended December 31, 2020	2019
License revenue	**$ 15,000,000**	$ —
Operating expenses		
Research and development	**12,594,823**	12,824,402
General and administrative	**8,762,222**	9,756,185
Restructuring expense	**—**	1,863,495
Total operating expenses	**21,357,045**	24,444,082
Loss from operations	**(6,357,045)**	(24,444,082)
Grant income	**1,813,976**	—
Other income	**79,900**	142,729
Interest income	**147,846**	1,030,839
Total other income	**2,041,722**	1,173,568
Net and comprehensive loss	**$ (4,315,323)**	$ (23,270,514)

Comparison of Years Ended December 31, 2020 and 2019

License Revenue

License revenue for the year ended December 31, 2020 of $15.0 million related to payment received as consideration pursuant to Amendment No. 1 of the Gossamer License Agreement. This revenue was recognized when cash was received upon execution of Amendment No. 1 on May 12, 2020. There were no milestones achieved related to the Gossamer License Agreement in 2020 or 2019.

No such license agreement amendment was executed in 2019.

Operating Expenses

The following table sets forth our operating expenses:

	Years Ended December 31, 2020	2019
Research and development	**$ 12,594,823**	$ 12,824,402
General and administrative	**8,762,222**	9,756,185
Restructuring expense	**—**	1,863,495
Total operating expenses	**$ 21,357,045**	$ 24,444,082

Research and Development

Research and development expenses for the year ended December 31, 2020, decreased $0.2 million, or 1.8%, compared to the year ended December 31, 2019. This was the result of decreased spending on clinical trials during 2020, specifically the Phase 2 program for glaucoma, and the I-SPY and RESCUE clinical trials, compared to the spending related to the completion of razuprotafib TIME-2b and glaucoma Phase 1b clinical trial during 2019.

General and Administrative

General and administrative expenses for the year ended December 31, 2020, decreased $1.0 million, or 10.2%, compared to the year ended December 31, 2019. This decrease was primarily attributable to a decrease in employee related expenses of $0.7 million, legal expenses of $0.3 million and general office expenses of $0.8 million related to the Company's restructuring efforts in 2019, offset by an increase in liability insurance of $0.3 million, consulting expense of $0.3 million and stock-based compensation of $0.2 million.

Restructuring Expense

Restructuring expenses for the year ended December 31, 2019 was $1.9 million and result of a reduction of headcount during 2019. No such actions were taken during 2020.

Other Income

The following table sets forth our other income:

	Years Ended December 31,	
	2020	**2019**
Other income	**$ 1,813,976**	$ —
Grant income	**79,900**	142,729
Interest income	**147,846**	1,030,839
Total other income	**$ 2,041,722**	$ 1,173,568

Other Income

Other income for the year ended December 31, 2020 of $1.8 million represents reimbursed internal and external qualified expenses related to the ARDS RESCUE clinical trial, per the terms of the MTEC arrangement. No such arrangement existed in 2019.

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 work performed. Grant income decreased in year ended December 31, 2020 compared to year ended December 31, 2019 primarily due to a grant awarded during 2019, and completed the middle of 2020, for development of ARP-1536. No new grants were awarded during 2020.

Interest Income

Interest income for the years ended December 31, 2020 and 2019, reflects interest earned on short term money market instruments. The net proceeds from our underwritten public offering in June 2018, sale of Company stock and payments received in conjunction with the execution of the Gossamer License Agreement in June 2018 and Amendment No. 1 in May 2020, less cash used in operations, were available for investment. The decrease in interest income in the year ended December 31, 2020 was due primarily to lower interest rates compared to prior year.

Liquidity and Capital Resources

Since inception, we have incurred significant net losses and negative cash flows from operations. For the years ended December 31, 2020 and 2019, we had net losses of $4.3 million and $23.3 million, respectively. At December 31, 2020 and 2019, we had an accumulated deficit of $146.6 million and $142.2 million, respectively.

At December 31, 2020, we had cash and cash equivalents of $42.6 million. To date, we have financed our operations principally through private and public offerings of our equity securities, private placements of our redeemable convertible preferred stock, common stock, issuances of secured convertible promissory notes and proceeds from the Amended Gossamer License Agreement and Amendment No. 1. Based on our current plans**,** we expect that our existing cash and cash equivalents, will enable us to conduct our planned operations through the fourth quarter of 2022.

In February 2018, we filed a shelf registration statement on Form S-3 with the SEC which was declared effective by the SEC on April 11, 2018 (the "Form S-3"). The shelf registration statement allows us to sell from time-to-time up to $150.0 million of common stock, preferred stock, debt securities, warrants, or units comprised of any combination of these securities, for our own account in one or more offerings. The shelf registration statement is intended to provide us flexibility to conduct registered sales of our securities, subject to market conditions and our future capital needs. The terms of any offering under the shelf registration statement will be established at the time of such offering and will be described in a prospectus supplement filed with the SEC prior to the completion of any such offering.

Additionally, on February 21, 2018, and pursuant to the Form S-3, we entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), pursuant to which we may issue and sell, from time to time, shares of our common stock having an aggregate offering price of up to $75.0 million through Cantor as our sales agent. Cantor may sell our common stock by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) of the Securities Act, including sales made directly on or through the Nasdaq Capital Market or any other existing trade market for our common stock, in negotiated transactions at market prices prevailing at the time of sale or at prices related to prevailing market prices, or any other method permitted by law. The shares of our common stock to be sold under the Sales Agreement will be sold and issued pursuant to the Form S-3 and the related prospectus and one or more prospectus supplements. We will pay Cantor 3.0% of the aggregate gross proceeds from each sale of shares of common stock under the Sales Agreement.

During the year ended December 31, 2020, 6,523,655 shares of common stock had been sold under this Sales Agreement and received net proceeds of $9.3 million, after deducting expenses of approximately $403,000 (including sales agent compensation of approximately $292,000) that were direct and incremental to the sale of the Company's common stock.

In January 2021, the Company initiated a process to explore a range of strategic alternatives focused on maximizing stockholder value from our clinical assets and cash resources. As part of this process, we are exploring strategic options for partnering our programs, as well as the potential for an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. There can be no assurance that this exploration of strategic alternatives will result in the Company entering or completing any transaction.

Ladenburg Thalmann & Co. Inc. and Duane Nash, M.D., J.D., M.B.A, have been retained with respect to the strategic review process.

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. Market volatility resulting from COVID-19 or other factors could also adversely impact our ability to access capital as and when needed. 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.

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

	Year Ended December 31, 2020	Year Ended December 31, 2019
Net cash used in operating activities	**$ (5,384,952)**	$ (23,852,522)
Net cash used in investing activities	**(19,025)**	(236,952)
Net cash provided by financing activities	**9,484,376**	—
Net increase (decrease) in cash and cash equivalents	**$ 4,080,399**	$ (24,089,474)

Operating Activities

We have historically experienced negative operating cash outflows as we developed razuprotafib and our pipeline programs. Our net cash used in operating activities primarily results from our net loss adjusted for non-cash expenses, changes in working capital components, amounts due to contract research organizations to conduct 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 by spending to advance and support our product candidates in the clinic and other operating and general administrative activities.

For the year ended December 31, 2020, operating activities used $5.4 million in cash primarily as a result of a net loss of $4.3 million, which includes $15.0 million of revenue earned from Amendment No. 1 to the Gossamer License Agreement, offset by $2.5 million in working capital and $1.4 million in non-cash expenses related to stock-based compensation and depreciation expense. We do not expect revenue will reoccur unless milestones outlined in the Gossamer License Agreement are achieved.

For the year ended December 31, 2019, operating activities used $23.9 million in cash primarily as a result of the net loss of $23.3 million offset by $1.9 million in working capital and $1.3 million in non-cash expenses related to stock-based compensation and depreciation expense.

Investing Activities

Net cash used in investing activities for the years ended December 31, 2020 and 2019 was related to capital expenditures to support operations.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 includes $9.3 million net proceeds from the sale of our common stock sold under the Sales Agreement with Cantor. No such activity occurred in 2019.

Contractual Obligations and Commitments

During 2019, the Company leased 7,580 square feet of office space in Cincinnati, Ohio, 4,000 square feet of office space in Lexington, Massachusetts and 687 square feet of office space in Dexter Michigan. During the fourth quarter of 2019, the Company terminated the Lexington and Dexter leases, without penalty. The Cincinnati property lease includes one month of free rent, escalating rent payments and expires in July 2021. Total rent expense for all operating leases was $0.2 million and $0.3 million for the years ended December 31, 2020 and 2019, respectively.

We also have 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 us upon written notice. In the event of a cancellation, we would be liable for the cost and expenses incurred to date as well as any close out costs of the service arrangement.

Off-Balance Sheet Arrangements

As of December 31, 2020 and 2019, we did not have any off-balance sheet arrangements as defined by applicable SEC regulations.

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 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. On an ongoing basis, we evaluate our estimates and judgments, including those related to prepaid and accrued research and development expenses, revenue recognition and stock-based compensation. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition

At the inception of an arrangement, the Company evaluates if a counterparty to a contract is a customer, if the arrangement is within the scope of revenue from contracts with customers guidance and the term of the contract. The Company recognizes revenue when its customer obtains control of promised goods or services in a contract for an amount that reflects the consideration the Company expects to receive in exchange for those goods or services. For contracts with customers, the Company applies the following five-step model in order to determine this amount: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. As part of the accounting for contracts with customers, the Company must develop assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. The Company then allocates the total transaction price to each performance obligation based on the estimated standalone selling prices of each performance obligation. The Company recognizes the amount of the transaction price as revenue that is allocated to the respective performance obligation when the performance obligation is satisfied or as it is satisfied.

The Company enters into collaboration arrangements, under which it licenses certain rights to its intellectual property to third parties. The terms of these agreements may include payment to the Company of one or more of the following: nonrefundable upfront license fees; development, sale and commercial milestone payments and royalties on net sales of licensed products. Each of these types of payments are classified as license revenue except for revenue from royalties on net sales of licensed products, which are classified as royalty revenue.

For each collaboration agreement that results in revenues, the Company identifies all material promised goods and services, which may include a license to intellectual property, research and development activities and/or transition activities. Promised goods or services are considered to be separate performance obligations if they are distinct. In order to determine the transaction price to be allocated to each performance obligation, in addition to any upfront payment, the Company estimates the amount of variable consideration at the outset of the contract either utilizing the expected value or most likely amount method, depending on the facts and circumstances relative to the contract. The Company constrains (reduces) the estimates of variable consideration such that it is probable that a significant reversal of previously recognized revenue will not occur throughout the life of the contract. When determining if variable consideration should be constrained, management considers whether there are factors outside the Company's control that could result in a significant reversal of revenue. In making these assessments, the Company considers the likelihood and magnitude of a potential reversal of revenue. These estimates are re-assessed each reporting period as required.

Once the estimated transaction price is established, amounts are allocated to the performance obligations that have been identified. The transaction price is generally allocated to each separate performance obligation on a relative standalone selling price basis. The Company must develop assumptions that require judgment to determine the standalone selling price ("SSP") in order to account for these agreements. To determine the standalone selling price the Company's assumptions may include (i) assumptions regarding the probability of obtaining marketing approval for the drug candidate; (ii) estimates regarding the timing of and the expected costs to develop and commercialize the drug candidate; (iii) estimates of future cash flows from potential product sales with respect to the drug candidate; and (iv) appropriate discount and tax rates. Standalone selling prices used to perform the initial allocation are not updated after contract inception. The Company does not include a financing component to its estimated transaction price at contract inception unless it estimates that certain performance obligations will not be satisfied within one year.

Upfront License and Amendment License Fees: If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from nonrefundable, upfront license and amendment license fees based on the relative value prescribed to the license compared to the total value of the arrangement. The revenue is recognized when the license is transferred to the collaborator and the collaborator is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, the Company applies an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, upfront license fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Development Milestone Payments: Depending on facts and circumstances, the Company may conclude it is appropriate to include the milestone in the estimated transaction price using the most likely amount method or it is appropriate to fully constrain the milestone. A milestone payment is included in the transaction price in the reporting period the Company concludes that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. The Company may record revenues from certain milestones in a reporting period before the milestone is achieved if the Company concludes that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. The Company records a corresponding contract asset when this conclusion is reached. Milestone payments that have not been included in the transaction price to date are fully constrained. These milestones remain fully constrained until the Company concludes that achievement of the milestone is probable and recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. The Company re-evaluates the probability of achievement of such development milestones and any related constraint each reporting period. The Company adjusts its estimate of the overall transaction price, including the amount of collaborative revenue that it has recorded, if necessary.

Sales-based Milestone and Royalty Payments: The Company's collaborators may be required to pay the Company sales-based milestone payments or royalties on future sales of commercial products. The Company recognizes revenues related to sales-based milestone and royalty payments upon the later to occur of (i) achievement of the collaborator's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming the license to the Company's intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate.

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:

- 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 amounts 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 Financial Accounting Standards Board ("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 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. 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.

For the years ended December 31, 2020 and 2019, stock-based compensation expense was $1.3 million and $1.1 million, respectively. As of December 31, 2020, we had $1.5 million of total unrecognized stock-based compensation costs for stock options, which we expect to recognize over a weighted-average period of 1.66 years.

JOBS Act Accounting Election

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

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.

We are a smaller reporting company, as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required by this Item.

Interest Rate Risk

The Company’s cash and cash equivalents at December 31, 2020 consist of all cash on hand, deposits and funds invested in short-term investments with original maturities of three months or less at the time of purchase and earn interest income. Therefore, there was minimal or no interest rate risk.

Item 8. Consolidated Financial Statements and Supplementary Data.

Beginning on page 80 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, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, stockholders' equity and cash flows for each of the two years in the period ended December 31, 2020, 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, 2020 and 2019, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

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 Company 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 11, 2021

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

AERPIO PHARMACEUTICALS, INC.

Consolidated Balance Sheets

	Year Ended December 31, 2020	2019
Assets		
Current assets:		
Cash and cash equivalents	**$ 42,604,935**	$ 38,524,536
Prepaid research and development contracts	**510,177**	311,154
Other current assets	**1,603,913**	734,785
Total current assets	**44,719,025**	39,570,475
Furniture and equipment, net	**121,730**	164,187
Operating lease right-of-use assets, net	**63,919**	162,124
Deposits	**20,000**	40,000
Total assets	**$ 44,924,674**	$ 39,936,786
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable and accrued expenses	**$ 1,799,371**	$ 3,231,450
Current portion of operating lease liability	**67,438**	102,555
Total current liabilities	**1,866,809**	3,334,005
Operating lease liability, net of current portion	**—**	67,438
Total liabilities	**1,866,809**	3,401,443
Commitments and contingencies (Note 10)		
Stockholders' equity:		
Common stock, $0.0001 par value per share; 300,000,000 shares authorized and 47,251,319 and 40,588,004 shares issued and outstanding at December 31, 2020 and 2019.	**4,725**	4,059
Additional paid-in capital	**189,603,985**	178,766,806
Accumulated deficit	**(146,550,845)**	(142,235,522)
Total stockholders' equity	**43,057,865**	36,535,343
Total liabilities and stockholders' equity	**$ 44,924,674**	$ 39,936,786

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,	
	2020	**2019**
License revenue	**$ 15,000,000**	$ —
Operating expenses		
Research and development	**12,594,823**	12,824,402
General and administrative	**8,762,222**	9,756,185
Restructuring expense	**—**	1,863,495
Total operating expenses	**21,357,045**	24,444,082
Loss from operations	**(6,357,045)**	(24,444,082)
Other income	**1,813,976**	—
Grant income	**79,900**	142,729
Interest income	**147,846**	1,030,839
Total other income	**2,041,722**	1,173,568
Net and comprehensive loss	**$ (4,315,323)**	$ (23,270,514)
Net and comprehensive loss per share		
Basic and diluted	**$ (0.10)**	$ (0.57)
Weighted average number of common shares used in computing net loss per share attributable to common stockholders, basic and diluted	**42,624,148**	40,588,004

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

AERPIO PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity

	Stockholders' Equity				
	Common Stock		Additional Paid-In	Accumulated	
	Shares	Par Value	Capital	Deficit	Total
Balance at December 31, 2019	40,588,004	$ 4,059	$ 177,621,807	$ (118,959,291)	$ 58,666,575
Issuance of warrants	—	—	53,440	—	53,440
Cumulative effect of change in accounting principle	—	—	5,717	(5,717)	—
Stock-based compensation expense	—	—	1,085,842	—	1,085,842
Net and comprehensive loss	—	—	—	(23,270,514)	(23,270,514)
Balance at December 31, 2019	40,588,004	4,059	$ 178,766,806	$ (142,235,522)	$ 36,535,343
Issuance of warrants	**—**	**—**	**71,939**	**—**	**71,939**
Issuance of common stock upon exercise of stock options	**139,660**	**14**	**143,520**	**—**	**143,534**
Issuance of common stock, net of issuance costs of $402,795	**6,523,655**	**652**	**9,340,190**	**—**	**9,340,842**
Stock-based compensation expense	**—**	**—**	**1,281,530**	**—**	**1,281,530**
Net and comprehensive loss	**—**	**—**	**—**	**(4,315,323)**	**(4,315,323)**
Balance at December 31, 2020	**47,251,319**	**$ 4,725**	**$ 189,603,985**	**$ (146,550,845)**	**$ 43,057,865**

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

AERPIO PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows

	Year Ended December 31, 2020	2019
Operating activities:		
Net and comprehensive loss	**$ (4,315,323)**	$ (23,270,514)
Adjustments to reconcile net and comprehensive loss to net cash used in operating activities:		
Depreciation	**61,482**	76,501
Loss on disposal of assets	—	94,713
Consulting expense related to warrants	**71,939**	53,440
Stock-based compensation	**1,281,530**	1,085,842
Changes in operating assets and liabilities:		
Prepaid research and development contracts	**(199,023)**	443,238
Other current assets	**(869,128)**	(119,104)
Deposits	**20,000**	960
Accounts payable and accrued expenses	**(1,436,429)**	(2,217,598)
Net cash used in operating activities	**(5,384,952)**	(23,852,522)
Investing activities:		
Purchase of furniture and equipment	**(19,025)**	(236,952)
Net cash used in investing activities	**(19,025)**	(236,952)
Financing activities:		
Proceeds from issuance of common stock	**9,743,637**	—
Cash paid in connection with the sale of common stock	**(402,795)**	—
Proceeds from issuance of common stock upon exercise of stock options	**143,534**	—
Net cash provided by financing activities	**9,484,376**	—
Net increase (decrease) in cash and cash equivalents	**4,080,399**	(24,089,474)
Cash and cash equivalents at beginning of year	**38,524,536**	62,614,010
Cash and cash equivalents at end of year	**$ 42,604,935**	$ 38,524,536

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

1. Nature of Organization and Operations

Aerpio Pharmaceuticals, Inc. ("Aerpio" or the "Company") is a biopharmaceutical company focused on developing compounds that activate Tie2 in indications in which the Company believes that activation of Tie2 may have therapeutic potential. Our product candidates include razuprotafib (formerly known as AKB-9778), a small molecule VE-PTP inhibitor. The Company was incorporated as Zeta Acquisition Corp. II ("Zeta") in the State of Delaware on November 16, 2007. Zeta was a "shell company" (as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended).

The Company's pipeline includes the following programs:

Glaucoma: Based on the preclinical proof of concept and the results of the Phase 1b trial showing a reduction in intraocular pressure ("IOP") in patients with ocular hypertension ("OHT") and open angle glaucoma ("OAG"), the Company initiated a Phase 2 clinical trial in June 2020 designed to evaluate the safety and efficacy of a topical formulation of razuprotafib in approximately 195 patients followed over a 28-day period. Patients enrolled in the trial were administered a baseline of latanoprost ophthalmic solution 0.005%, and then randomized in a 1:1:1 fashion to receive adjunctive therapy consisting of placebo, 40 mg/ml razuprotafib once-daily, or 40 mg/ml razuprotafib twice-daily. The primary endpoint of the study was mean diurnal IOP at 28 days in the razuprotafib treated groups compared to the latanoprost monotherapy group.

In December 2020, the Company reported that razuprotafib met the primary efficacy endpoint at the end of the 28-day period ("Day 28") with the twice-daily ("BID") dose group in its double-blind, placebo-controlled Phase 2 trial in patients with elevated IOP associated with OAG or OHT. The change from baseline in diurnal mean IOP at Day 28 of study eyes treated with razuprotafib BID plus latanoprost showed a statistically significant improvement, or drop in IOP, (two-sided p-value 0.0130 and LS mean difference of -0.92 mm Hg) compared to those treated with latanoprost monotherapy. The razuprotafib once-daily dose group did not show a statistically significant improvement at Day 28. While the Phase 2 clinical trial met its primary efficacy endpoint with the BID group, the IOP decrease was not at a level deemed sufficient to move to Phase 3 development.

Acute Respiratory Distress Syndrome: Based on results in preclinical studies and observations in patients in the TIME-2 and TIME-2b trials, the Company believes that a vascular endothelial receptor, Tie2, may play a pivotal role in the defense against microvascular breach in ARDS. The Company hypothesizes that razuprotafib, the Company's lead Tie2 activator, may have therapeutic potential for the treatment of COVID-19 associated ARDS and initiated two Phase 2 trials during 2020.

In May 2020, the Company was selected by Quantum Leap Healthcare Collaborative to participate in the I-SPY COVID-19 Trial (Investigation of Serial studies to Predict Your COVID Therapeutic Response with biomarker Integration and Adaptive Learning) to evaluate subcutaneous razuprotafib for the treatment of COVID-19 related ARDS in adult patients with critical COVID-19. The trial was initiated during the third quarter of 2020 and trial updates are anticipated in the first half of 2021, subject to potential delays in subject enrollment and study completion, including due to delays arising from the ongoing COVID-19 pandemic, and the potential for project cancellation or discontinuation by Quantum Leap Healthcare Collaborative.

In August 2020, the Company initiated a second Phase 2 clinical trial ("RESCUE") for the treatment of COVID-19 with the U.S. Government operating through Medical Technology Enterprise Consortium ("MTEC"). This RESCUE trial will evaluate subcutaneous razuprotafib for the prevention and treatment of ARDS in adult patients with moderate to severe COVID-19 as part of MTEC-20-09-COVID-19 Treatment Military Infectious Disease Research Program ("MIDRP") "Development of Treatments for COVID-19". Per the terms of the agreement with MTEC, MTEC will provide partial reimbursement up to $5.1 million related to qualified internal and external spending of the Company, as it relates to the clinical trial. The Company expects to report top-line data upon study completion in the second quarter of 2021.

Diabetic Kidney Disease: In two consecutive trials, TIME-2 and TIME-2b, subcutaneous razuprotafib showed reduction in Urine Albumin-Creatinine Ratio ("UACR"), a measure of progression of diabetic kidney disease. The Company believes that systemic treatment with razuprotafib 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.

ARP-1536 and Bi-specific Antibody: The humanized monoclonal antibody, ARP-1536, directed at the same target as subcutaneous razuprotafib, is in preclinical development. The Company is evaluating development options for ARP-1536, including subcutaneous injection for the treatment of diabetic vascular complications, e.g., diabetic nephropathy and intravitreal injection as an adjunctive therapy for diabetic macular edema. The Company is also developing a bispecific antibody that binds both vascular endothelial growth factor ("VEGF") and vascular endothelial protein tyrosine phosphatase ("VE-PTP") which is designed to inhibit VEGF activation and activate Tie2. The Company believes this bispecific antibody has the potential to be an improved treatment for wet aged-related macular degeneration ("AMD") and diabetic macular edema via intravitreal injection.

In June 2018, the Company licensed AKB-4924 (now GB004), a selective stabilizer of hypoxia-inducible factor-1 alpha ("HIF-1 alpha") to a wholly-owned subsidiary of Gossamer Bio, Inc., GB004, Inc. (collectively "Gossamer"), which is being developed for the treatment of inflammatory bowel disease ("IBD"). HIF-1 alpha is involved in mucosal wound healing and the reduction of inflammation in the gastrointestinal tract. Gossamer completed the Phase 1b clinical trial in ulcerative colitis ("UC") patients and reported results during the second quarter of 2020. Gossamer has announced that, subject to developments in the ongoing COVID-19 pandemic, it initiated a 12-week Phase 2 study of GB004 in patients with mild-to-moderate UC during the second half of 2020.

In May 2020, the Company received a one-time payment of $15.0 million pursuant to an amendment to its license agreement with Gossamer resulting in a reduction in future potential milestone payments and tiered royalty rates over the life of the license agreement. Gossamer is responsible for all remaining development and commercial activities for GB004.

In February 2018, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission ("SEC") which was declared effective by the SEC on April 11, 2018 (the "Form S-3"). On February 21, 2018, and pursuant to the Form S-3, the Company entered into a Controlled Equity Offering Sales Agreement (the "Sales Agreement") with Cantor Fitzgerald & Co. ("Cantor"), pursuant to which it may issue and sell, from time to time, shares of its common stock having an aggregate offering price of up to $75.0 million through Cantor as the sales agent. Cantor may sell the Company's common stock by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) of the Securities Act, including sales made directly on or through the Nasdaq Capital Market or any other existing trade market for the Company's common stock, in negotiated transactions at market prices prevailing at the time of sale or at prices related to prevailing market prices, or any other method permitted by law. During the year ended December 31, 2020, 6,523,655 shares of the Company's common stock were sold under the Sales Agreement, pursuant to the Form S-3, the related prospectus, and the prospectus supplement. The net proceeds received from this transaction were $9.3 million, after deducting expenses of approximately $403,000 (including sales agent compensation of approximately $292,000) that were direct and incremental to the sale of the Company's common stock.

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's revenue has been primarily limited to license revenue from Gossamer described in Note 14. 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 pipeline products that are approved, and protection of proprietary technology. If the Company does not successfully commercialize any of its pipeline products or mitigate any of these other risks, it will be unable to generate revenue or achieve profitability.

The Company incurred losses from operations and had negative cash flows from operating activities for the year ended December 31, 2020 and 2019 (and since inception). As of December 31, 2020, the Company's cash and cash equivalents were approximately $42.6 million. The company is currently evaluating its development options for its product candidates. Any efforts for continued program development will be time-consuming and expensive. Based on its current operating plan, and absent any future financings or strategic partnerships, the Company believes its existing cash and cash equivalents will be sufficient to fund its current operating plan through the fourth quarter of 2022, and as a result, through at least twelve months from the filing of the Company's 2020 Annual Report on Form 10-K.

There can be no assurance, however, that the current operating plan will be achieved in the time frame anticipated by the Company, or that its cash resources will fund the Company's operating plan for the period anticipated by the Company or that additional funding will be available on terms acceptable to the Company, or at all. Market volatility resulting from the COVID-19 pandemic or other factors could also adversely impact the Company's ability to access capital as and when needed. If the Company is unable to raise the necessary funds when needed on a timely basis, it may be required to suspend its operations.

The Company is currently evaluating a range of strategic alternatives focused on maximizing stockholder value from its clinical assets and cash resources. As part of this process, it is exploring strategic options for partnering its programs, as well as the potential for an acquisition, company sale, merger, business combination, asset sale, in-license, out-license or other strategic transaction. There can be no assurance that this exploration of strategic alternatives will result in the Company entering or completing any transaction.

COVID-19 has resulted, and will likely continue to result, in significant governmental measures being implemented to control the spread of the virus through quarantines, travel restrictions, heightened border security and other measures. While the Company cannot predict the scope and severity, these developments and measures could materially and adversely affect its business, including its clinical trials for ARDS programs, results of operations and financial condition. In addition, in response to the continuing spread of COVID-19, the Company has kept its executive offices closed with its employees continuing their work outside of the office. The Company is closely monitoring the impact of COVID-19 on all aspects of its business and is taking steps to minimize the impact on its business. However, the extent to which COVID-19 ultimately impacts the Company's business, results of operations or financial condition will depend on future developments, which remain highly uncertain and cannot be predicted with confidence, such as the duration of the COVID-19 pandemic, new information that may emerge concerning the severity of COVID-19 and the effectiveness of actions taken to contain the COVID-19 pandemic or treat its impact, among others. While some states and jurisdictions have started to rollback stay-at-home and quarantine orders and reopened in phases, it is difficult to predict what the lasting impact of the COVID-19 pandemic will be, and if the Company or any of the third parties with whom it engages were to experience additional shutdowns or other prolonged business disruptions, the Company's ability to conduct its business in the manner and on the timelines presently planned could have a material adverse impact on the Company's business, results of operation and financial condition. In addition, a recurrence of COVID-19 cases could cause other widespread or more severe impacts depending on where infection rates are highest. The Company will continue to monitor developments as it deals with the disruptions and uncertainties relating to the COVID-19 pandemic.

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in accordance with SEC regulations and include all of the information and disclosures required by U.S. generally accepted accounting principles ("U.S. GAAP" or "GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

The Company's consolidated financial statements are stated in U.S. Dollars.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company views its operations and manages its business in one operating segment, which is the business of developing and commercializing proprietary therapeutics. All the assets and operations of the Company's sole operating segment are located in the United States.

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 revenue and expenses during the reporting period. Actual results may differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies and controls, and in developing the estimates and assumptions that are used in the preparation of these 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: prepaid and accrued research and development expense, stock-based compensation expense, revenue recognition and income taxes.

The Company's results can also be affected by economic conditions, global health concerns, such as COVID-19, and 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 and $100,000 invested in short-term certificates of deposits with original maturities of three months or less at the time of purchase. At December 31, 2020 and 2019, the Company's cash equivalents are primarily held in money market funds. The Company maintains balances with its banks in excess of federally insured limits.

Revenue Recognition

At the inception of an arrangement, the Company evaluates if a counterparty to a contract is a customer, if the arrangement is within the scope of revenue from contracts with customers guidance and the term of the contract. The Company recognizes revenue when its customer obtains control of promised goods or services in a contract for an amount that reflects the consideration the Company expects to receive in exchange for those goods or services. For contracts with customers, the Company applies the following five-step model in order to determine this amount: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. As part of the accounting for contracts with customers, the Company must develop assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. The Company then allocates the total transaction price to each performance obligation based on the estimated standalone selling prices of each performance obligation. The Company recognizes the amount of the transaction price as revenue that is allocated to the respective performance obligation when the performance obligation is satisfied or as it is satisfied.

The Company enters into collaboration arrangements, under which it licenses certain rights to its intellectual property to third parties. The terms of these agreements may include payment to the Company of one or more of the following: nonrefundable upfront license fees; development, sale and commercial milestone payments and royalties on net sales of licensed products. Each of these types of payments are classified as license revenue except for revenue from royalties on net sales of licensed products, which are classified as royalty revenue, if received.

For each collaboration agreement that results in revenues, the Company identifies all material promised goods and services, which may include a license to intellectual property, research and development activities and/or transition activities. Promised goods or services are considered to be separate performance obligations if they are distinct. In order to determine the transaction price to be allocated to each performance obligation, in addition to any upfront payment, the Company estimates the amount of variable consideration at the outset of the contract either utilizing the expected value or most likely amount method, depending on the facts and circumstances relative to the contract. The Company constrains (reduces) the estimates of variable consideration such that it is probable that a significant reversal of previously recognized revenue will not occur throughout the life of the contract. When determining if variable consideration should be constrained, management considers whether there are factors outside the Company's control that could result in a significant reversal of revenue. In making these assessments, the Company considers the likelihood and magnitude of a potential reversal of revenue. These estimates are re-assessed each reporting period as required.

Once the estimated transaction price is established, amounts are allocated to the performance obligations that have been identified. The transaction price is generally allocated to each separate performance obligation on a relative standalone selling price basis. The Company must develop assumptions that require judgment to determine the standalone selling price ("SSP") in order to account for these agreements. To determine the standalone selling price the Company's assumptions may include (i) assumptions regarding the probability of obtaining marketing approval for the drug candidate; (ii) estimates regarding the timing of and the expected costs to develop and commercialize the drug candidate; (iii) estimates of future cash flows from potential product sales with respect to the drug candidate; and (iv) appropriate discount and tax rates. Standalone selling prices used to perform the initial allocation are not updated after contract inception. The Company does not include a financing component to its estimated transaction price at contract inception unless it estimates that certain performance obligations will not be satisfied within one year.

Upfront License and Amendment License Fees: If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from nonrefundable, upfront (or one-time) license and amendment license fees based on the relative value prescribed to the license compared to the total value of the arrangement. The revenue is recognized when the cash is received or when the license is transferred to the collaborator and the collaborator is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, the Company applies an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, license fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Development Milestone Payments: Depending on facts and circumstances, the Company may conclude it is appropriate to include the milestone in the estimated transaction price using the most likely amount method or it is appropriate to fully constrain the milestone. A milestone payment is included in the transaction price in the reporting period the Company concludes that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. The Company may record revenues from certain milestones in a reporting period before the milestone is achieved if the Company concludes that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. The Company records a corresponding contract asset when this conclusion is reached. Milestone payments that have not been included in the transaction price to date are fully constrained. These milestones remain fully constrained until the Company concludes that achievement of the milestone is probable and recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. The Company re-evaluates the probability of achievement of such development milestones and any related constraint each reporting period. The Company adjusts its estimate of the overall transaction price, including the amount of collaborative revenue that it has recorded, if necessary.

Sales-based Milestone and Royalty Payments: The Company's collaborators may be required to pay the Company sales-based milestone payments or royalties on future sales of commercial products. The Company recognizes revenues related to sales-based milestone and royalty payments upon the later to occur of (i) achievement of the collaborator's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming the license to the Company's intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate.

Other Income

Other income represents reimbursed internal and external qualified expenses, per the terms of the MTEC arrangement, related to the ARDS clinical trial. Other income is recorded, and generally received, in the period the internal or external qualified clinical trial expenses are incurred, and paid, by the Company.

Grant Income

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

Research and Development

Research and development costs 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; and (iv) costs associated with clinical, preclinical and regulatory activities.

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 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 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, 2020 and 2019, the Company does not have any uncertain tax positions. The Company recognizes interest and penalties related to uncertain tax positions, if any exist, in income tax expense.

Net and Comprehensive Loss per Share Attributable to Common Stockholders

The Company's basic net and comprehensive loss per share attributable to common stockholders is calculated by dividing the net and comprehensive loss by the weighted average number of shares of common stock outstanding for the period. The diluted net and comprehensive 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.

Stock-Based Compensation

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation – Stock Compensation* (“ASC 718”). ASC 718 requires all stock-based payments to employees, including grants of employee stock options, 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 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.

Due to the historical 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.

Fair Value of Financial Instruments

The Company’s financial instruments consist of cash and cash equivalents, accounts payable and accrued expenses. The Company values cash equivalents using quoted market prices. The fair value of accounts payable and accrued expenses approximates its carrying value because of its 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. 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, 2020 and 2019. The assets of the Company measured at fair value on a recurring basis as of December 31, 2020 and 2019 are summarized below:

	Fair Value Measurements Using			
	Level 1	**Level 2**	**Level 3**	**Total**
December 31, 2020				
Assets:				
Cash and cash equivalents	**$ 42,604,935**	**$ —**	**$ —**	**$ 42,604,935**
Total assets	**$ 42,604,935**	**$ —**	**$ —**	**$ 42,604,935**
December 31, 2019				
Assets:				
Cash and cash equivalents	$ 38,524,536	$ —	$ —	$ 38,524,536
Total assets	$ 38,524,536	$ —	$ —	$ 38,524,536

Concentrations of Credit Risk and Off-Balance Sheet Risk

Cash and cash equivalents are the only financial instruments that potentially subject the Company to concentrations of credit risk. At December 31, 2020 and 2019, the Company maintains its cash and cash equivalents with high-quality, accredited financial institutions and, accordingly, such funds are subject to minimal credit risk. The Company has no 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).

Leases

At the inception of an arrangement the Company determines whether the arrangement is or contains a lease based on the circumstances present. All leases with a term greater than one year are recognized on the consolidated balance sheet as right-of-use assets, net, lease liabilities and, if applicable, long-term lease liabilities. The Company has elected not to recognize on the consolidated balance sheet leases with terms of one-year or less if entered into. Lease liabilities and their corresponding right-of-use assets, net are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable. As such, the Company utilizes the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Certain adjustments to the right-of-use assets, net may be required for items such as initial direct costs paid or incentives received.

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 financial position or results of operations upon adoption.

In June 2018, the FASB issued ASU 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 improves financial reporting for share-based payments issued to nonemployees under ASC 718 by expanding the scope of the employee share-based payments guidance to include share-based payments issued to nonemployees. The amendments in ASU 2018-07 were effective for public companies for fiscal years beginning after December 31, 2018, including interim periods within that fiscal year. The Company adopted ASU 2018-07 as of January 1, 2019 and recorded a one-time cumulative adjustment of $5,717 upon adoption.

No other new accounting pronouncement recently issued or newly effective had or is expected to have a material impact on the Company's consolidated financial statements.

3. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses consist of the following as of:

	December 31,	
	2020	**2019**
Accounts payable	**$ 523,037**	$ 439,785
Accrued bonus	**428,683**	689,830
Professional fees	**444,534**	346,999
Accrued project costs	**328,463**	382,131
Accrued vacation	**48,107**	43,470
Restructuring accrual (see Note 15)	**—**	793,913
Accrued retention bonus	**—**	521,859
Other	**26,547**	13,463
Total accounts payable and accrued expenses	**$ 1,799,371**	$ 3,231,450

4. Furniture and Equipment

Furniture and equipment consist of the following as of:

	December 31,	
	2020	**2019**
Furniture	**$ 154,669**	$ 154,669
Computers	**68,642**	56,443
Equipment	**252,882**	246,056
Leasehold improvements	**35,869**	35,869
Total furniture and equipment	**512,062**	493,037
Accumulated depreciation	**(390,332)**	(328,850)
Furniture and equipment, net	**$ 121,730**	$ 164,187

5. Common Stock

As of December 31, 2020 and 2019, the Company had 300,000,000 shares of authorized common stock with par value of $0.0001 per share.

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 of the Company (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.

Warrants to Purchase Common Stock

At December 31, 2020 and 2019, the Company had warrants outstanding for the purchase of 600,000 and 917,562 shares, respectively, of the Company's common stock. In October 2019, the Company issued warrants for the purchase of 600,000 shares of the Company's common stock at an exercise price of $0.486 per share in connection with the hiring of a strategic advisor consultant for a six-month period. These warrants vested in equal monthly installments over a six-month period beginning October 14, 2019 and expire on October 24, 2024. At the date of grant the fair value of these awards was determined using a Black-Scholes Merton pricing model. Included at December 31, 2019, are warrants for the purchase of 317,562 shares of the Company's common stock at an exercise price of $5.00 per share that were issued in 2017 and have a three-year term. The 317,562 warrants expired on March 15, 2020, and none were exercised or settled as the fair value of the Company's common stock was below the exercise price. The number of shares and the exercise price shall be adjusted for standard anti-dilution events such as stock splits, combinations, reorganizations, or issue shares as part of a stock dividend. Upon a change of control, the warrant holder will have the right to receive securities, cash or other properties it would have been entitled to receive had the warrant been exercised. The warrants are equity classified instruments and do not contain contingent exercise provisions, or other features, that would preclude the Company from concluding that the warrants are indexed solely to the Company's common stock.

6. Preferred Stock

As of December 31, 2020 and 2019, 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, 2020 and 2019.

7. Stock-Based Compensation

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 Company's 2011 Equity Incentive 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. As a result of the evergreen increase, a total of 1,623,520 shares were added to the 2017 Plan on January 1, 2020 and a total of 1,890,052 were added to the 2017 Plan on January 1, 2021.

Stock Options

The options granted generally vest over 48 months. Under the 2017 Plan, options vest in installments of 25% at the one-year anniversary and thereafter in 36 equal monthly installments beginning on the 1st of the month after the one-year anniversary date, subject to the employee's continuous service with the Company. In May 2019, the Company issued a special retention grant of options to purchase an aggregate of 2,419,050 shares of common stock which vest in installments of 50% at June 30, 2020 and 50% at June 30, 2021, 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. Option awards to purchase an aggregate of 962,720 and 4,666,728 shares of common stock were granted during the year ended December 31, 2020 and 2019, respectively. All option awards granted during 2020 and 2019 were under the 2017 Equity Plan.

As of December 31, 2020 and 2019, 3,634,905 and 1,983,093 shares were reserved for issuance under the 2017 Plan, respectively.

The following table summarizes the stock option activity during the years ended December 31, 2020 and 2019:

	Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value
Outstanding, January 1, 2019	3,351,132	$ 3.73	8.24	$ 142,788
Granted	4,666,728	1.85		
Exercised	—			
Expired/cancelled	(2,682,010)	2.70		
Outstanding, December 31, 2019	5,335,850	$ 2.60	6.23	$ 2,866
Expected to vest, December 31, 2019	2,395,265	$ 1.93	9.00	$ 2,866
Options exercisable, December 31, 2019	2,940,585	$ 3.15	3.98	$ —
Outstanding, January 1, 2020	5,335,850	$ 2.60	6.23	$ 2,866
Granted	962,720	0.71		
Exercised	(139,660)	1.03		
Expired/cancelled	(1,516,670)	3.97		
Outstanding, December 31, 2020	4,642,240	$ 1.81	7.00	$ 358,209
Expected to vest, December 31, 2020	2,142,687	$ 1.45	8.55	$ 333,028
Options exercisable, December 31, 2020	2,499,553	$ 2.12	5.67	$ 25,181

Aggregate intrinsic value represents the estimated fair value of the Company’s common stock 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, 2020 and 2019, was $358,209 and $2,866, respectively.

Stock options exercised during 2020 had an intrinsic value of $149,172. No stock options were exercised during 2019.

For the years ended December 31, 2020 and 2019, the Company recognized compensation expense for stock options of $1,281,530 and $1,085,842, respectively. During the fourth quarter of 2019, the Company recorded a one-time stock-based compensation cumulative reversal of $1,051,735 for the forfeitures of outstanding equity awards related to the Chief Executive Officer and Chief Financial and Business Officer who departed the Company on October 15, 2019. As of December 31, 2020, there was $1,463,227 of unrecognized compensation cost related to stock options, which is expected to be recognized over a weighted average period of 1.66 years.

The Company uses the Black-Scholes option pricing model to determine the estimated fair value for stock-based awards. For the years ended December 31, 2020 and 2019, there were 962,720 and 4,666,728 options granted out of the 2017 Plan, respectively. Option pricing models require the input of various assumptions, including the option's expected life, expected dividend yield, price volatility and risk-free interest rate of the underlying stock. As there has not 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, 2020 and 2019, was $0.43 and $1.11, respectively. The calculation was based on the following assumptions.

	Year Ended December 31, 2020	2019
Expected term (years)	**5.92**	5.36
Risk-free interest rate	**0.53%**	2.24%
Expected volatility	**69.36%**	64.88%
Expected dividend yield	—	—

Compensation Expense Summary

The Company recognized the following compensation cost related to employee and non-employee stock-based compensation activity for the periods presented below.

	Year Ended December 31, 2020	2019
Research and development	**$ 537,515**	$ 510,923
General and administrative	**744,015**	574,919
Total	**$ 1,281,530**	$ 1,085,842

The increase in compensation expense during the year ended December 31, 2020, is primarily due to expense related to the May 2019 special retention grant.

8. Income Taxes

The Company did not record a current or deferred income tax expense or benefit for the years ended December 31, 2020 and 2019, due to the Company's net and comprehensive losses and increases in its deferred tax asset valuation allowance. A reconciliation of the statutory federal income tax with the provision for income taxes are as follows:

	Year Ended December 31, 2020	2019
Federal tax at statutory rate	**(21.00%)**	(21.00%)
State and local tax at statutory rates, net of federal income tax	**(6.52)**	(0.82)
Research and development credits	**(15.90)**	(3.39)
Stock-based compensation	**13.31**	0.49
Other	**0.04**	0.07
Change in valuation allowance	**30.07**	24.65
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, 2020	December 31, 2019
Deferred tax assets:		
Net operating loss carryforwards	**$ 26,184,326**	$ 24,966,019
Accrued expenses	**107,525**	413,048
Stock-based compensation	**428,125**	738,768
Research and development credits	**5,326,964**	4,640,960
Operating lease right-of-use assets, net	**15,152**	37,793
Other	**5,232**	2,423
Total deferred tax assets	**32,067,324**	30,799,011
Deferred tax liabilities:		
Furniture and equipment	**17,425**	24,967
Operating lease liability	**14,361**	36,044
Total deferred tax liabilities	**31,786**	61,011
Net deferred tax assets before valuation allowance	**32,035,538**	30,738,000
Less valuation allowance	**(32,035,538)**	(30,738,000)
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 increased $1,297,538 and $5,735,658 in 2020 and 2019, respectively, as a result of an increase in the net operating loss ("NOL") and an increase of 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, 2020, the Company has $84,173,001 of federal NOL carryforwards with expirations between 2032 and 2038. The Company has $33,263,905 of federal NOL carryforwards with no expiration as a result of the 2017 Tax Act. Additionally, the Company has $64,932,119 of state and local NOL carryforwards with expiration between 2021 and 2041. Finally, at December 31, 2020, the Company has $5,326,964 of federal research and development credit carryforwards that expire at various dates through 2041.

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 until fully utilized. 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. A full valuation allowance has been provided against the Company's NOL and tax credit carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the deferred tax asset established for the NOL and tax credit carryforwards and the valuation allowance.

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, 2020 and 2019, 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.

9. Net and Comprehensive Loss per Share Attributable to Common Stockholders

The following table sets forth the computation of the Company's basic and diluted net and comprehensive loss per share attributable to common stockholders for the periods presented:

	Year Ended December 31, 2020	Year Ended December 31, 2019
Net and comprehensive loss attributable to common stockholders	**$ (4,315,323)**	$ (23,270,514)
Weighted average common shares used in computing net and comprehensive loss per share attributable to common stockholders, basic and diluted	**42,624,148**	40,588,004
Net and comprehensive loss per share attributable to common stockholders, basic and diluted	**$ (0.10)**	$ (0.57)

The following weighted average common stock equivalents were excluded from the calculation of diluted net and comprehensive loss per share for the year ended December 31, 2020 and 2019, because including them would have had an anti-dilutive effect:

	Year Ended December 31, 2020	Year Ended December 31, 2019
Options to purchase common stock	**4,642,240**	5,335,850
Warrants to purchase common stock	**600,000**	917,562

10. Leases

At December 31, 2020, the Company is a party to one property lease in Cincinnati, Ohio under an arrangement which provides the right to use the underlying asset and require lease payments for the lease term. During the fourth quarter of 2019, the Company terminated its leases in Lexington, Massachusetts and Dexter, Michigan; no penalties were incurred related to these terminations. The Cincinnati, Ohio lease agreement obligates the Company to pay real estate taxes, insurance and certain maintenance costs (hereinafter referred to as non-lease components). The Company's lease arrangement contains a renewal provision of 5 years, exercisable at the Company's option. The Company's lease agreement does not contain any material residual value guarantees or material restrictive covenants.

The Company determines if an arrangement is an operating lease at inception. Leases with an initial term of 12 months or less are not recorded on the consolidated balance sheet. All other leases are recorded on the consolidated balance sheet with a corresponding operating lease asset, net, representing the right to use the underlying asset for the lease term and the operating lease liabilities representing the obligation to make lease payments arising from the lease.

Operating lease assets and operating lease liabilities are recognized at commencement date based on the present value of lease payments over the lease term and include options to extend or terminate the lease when they are reasonably certain to be exercised. The present value of lease payments is determined primarily using the incremental borrowing rate based on the information available at lease commencement date. Lease agreements with lease and non-lease components are generally accounted for as a single lease component. The Company's operating lease expense is recognized on a straight-line basis over the lease term and are recorded in general and administrative expenses on the consolidated statements of operations and comprehensive loss.

The following table presents the lease cost and information related to the right-of-use assets, net and operating lease liabilities:

	Year Ended December 31, 2020	2019
Lease cost		
Average rent expense	**$ 113,429**	$ 242,690
Other information		
Cash paid for amounts included in the measurement of operating lease liabilities	**$ 117,780**	$ 242,581
The weighted average remaining lease term and discount rate at December 31, 2020		
Weighted-average remaining lease term - operating leases	0.58	
Weighted-average discount rate - operating leases	13.28%	

As of December 31, 2020, future payments related to operating leases activities are presented in the table below:

	2021	2022	2023 and Thereafter	Total
Operating leases	**$ 69,685**	$ —	$ —	$ 69,685
Less interest				(2,247)
Present value of lease liabilities				$ 67,438

11. Employee Retirement Plan

The Company maintains a 401(k) plan (the "401k Plan") created in 2015 for the benefit of its employees. All employees who have attained the age of 21 are eligible to participate in the 401k Plan as of the first Entry Date, as defined by the 401k Plan document, 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. No contributions were made during 2020 or 2019.

12. Employee Bonus Plan

The Company maintains a bonus plan for certain employees based on the achievement of certain goals and milestones. At December 31, 2020 and 2019, the Company accrued $428,683 and $689,830, respectively, for bonuses.

13. Employee Stock Purchase Plan

In March 2017, the Board of Directors adopted and the stockholders approved the Employee Stock Purchase Plan that became effective in April 2017. On June 20, 2018, the Company's shareholders approved the Amended and Restated 2017 Employee Stock Purchase Plan ("ESPP") at the Annual Meeting of Shareholders. Pursuant to the terms of the ESPP, the Company will reserve for issuance 300,000 shares of the Company's common stock in the aggregate, plus, on January 1, 2019 and each January 1 thereafter through January 1, 2028, the number of shares of the Company's common stock reserved and available for issuance under the ESPP will be cumulatively increased by the least of (i) one percent of the number of shares of the Company's common stock issued and outstanding on the immediately preceding December 31; (ii) 350,000 shares; or (iii) such lesser number of shares of the Company's common stock as determined by the Board of Directors, in each case subject to adjustment in accordance with the terms of the ESPP. In March 2020, the Company's Board of Directors approved an increase of 350,000 shares to the SEPP, which increase was effective as of January 1, 2020. No shares under the ESPP are outstanding at December 31, 2020 and 2019.

14. License Agreement

On June 24, 2018, the Company entered into a License Agreement (the "Gossamer License Agreement") with Gossamer, under which the Company granted Gossamer an exclusive, sublicensable license to develop and commercialize AKB-4924 and other structurally related products worldwide, with initial development expected in the indications of induction and maintenance in ulcerative colitis and Crohn's Disease (collectively "initial indications"). Prior to the execution of the Gossamer License Agreement, AKB-4924 was a pipeline program for the Company that completed a Phase 1a clinical trial in healthy volunteers.

On May 12, 2020, the Company entered into Amendment No. 1 to the Gossamer License Agreement ("Amendment No. 1"). Pursuant to Amendment No. 1, Gossamer made a payment to the Company of $15.0 million on May 12, 2020. For the year ended December 31, 2020, the Company recognized revenue of $15.0 million based on the terms of Amendment No. 1, and no such revenue was recognized during the year ended December 31, 2019.

Gossamer is responsible for the development and commercialization of the licensed products, and a joint development committee has been formed to oversee the development and manufacturing activities related to the licensed products. Under the terms of the Gossamer License Agreement and as amended by Amendment No. 1 (collectively, the "Amended Gossamer License Agreement"), Gossamer is obligated to use its commercially reasonable efforts to develop and commercialize licensed products in the United States, two major European countries and Japan for at least one of the initial indications. The Amended Gossamer License Agreement includes an exclusivity provision that prohibits the Company from developing, manufacturing or commercializing, and prohibits Gossamer from clinically developing or commercializing certain HIF stabilizing compounds other than as permitted in the Amended Gossamer License Agreement.

Under the terms of the Amended Gossamer License Agreement, the Company is eligible to receive up to $40.0 million in approval milestone payments related to indications in ulcerative colitis and Crohn's disease, and up to $50.0 million in sales milestone payments. The Company is also eligible to receive the tiered royalties on sales of licensed products from percentages ranging from a low-single-digit to mid-single-digit, subject to certain customary reductions.

In addition, under certain circumstances, in lieu of receiving the foregoing milestone payments and royalties, the Company may elect to receive 20% of payments received by Gossamer and its stockholders (with some exclusions) in connection with Gossamer's grant of a sublicense or other rights to the licensed products or if Gossamer undergoes a changes of control and the value of the transaction exceeds a certain value (provided that Gossamer can prevent the Company from exercising this option if the parent company of Gossamer is the entity undergoing the change of control, in which case each of the royalty rate percentages described above would automatically be increased by low single digits). Conversely, the Company could be required to accept such 20% of those payments if Gossamer agrees to pay the Company a certain minimum upon Gossamer and its stockholders being paid. Such amount may be reduced if the transaction includes pharmaceutical candidates or products or other named asset categories in addition to the licensed products.

The Amended Gossamer License Agreement expires on a licensed-product-by-licensed-product and country-by-country basis on the later of fifteen years from the date of first commercial sale or when there is no longer a valid patent claim covering such licensed product in such country. Either party may terminate the Amended Gossamer License Agreement for an uncured material breach by the other party or upon the bankruptcy or insolvency of the other party. Gossamer may terminate the Amended Gossamer License Agreement in the event Gossamer determines there is a potential safety or efficacy issue with the licensed products. The Company may terminate the amended Gossamer License Agreement if Gossamer institutes certain actions related to the licensed patents. Under certain termination circumstances, the Company would have worldwide rights to the terminated program.

As of December 31, 2020, all development milestones, sales-based milestones and royalty payments within the Amended Gossamer License Agreement are constrained to the point where no transaction price has been allocated to the future milestones or royalty payments.

15. Restructuring

In April 2019, the Company executed a realignment plan to reduce operating costs and better align its workforce with the needs of its ongoing business. The realignment plan reduced the Company’s workforce by 11 employees, representing approximately 41% of its workforce. Additionally, in October 2019, the Company’s Chief Executive Officer and Chief Financial Officer departed from their positions. As a result of these reductions, the Company recorded employee severance expense of $1.9 million during the year ended December 31, 2019. These amounts are included within restructuring expense in the consolidated statements of operations and comprehensive loss.

Total cash payments against the severance liability was approximately $0.8 million in the year ended December 31, 2020. There is no remaining liability as of December 31, 2020.

16. Subsequent Events

On January 29, 2021, the Company executed a realignment plan to reduce operating costs and better align its workforce with the needs of its ongoing business. The realignment plan reduces its current workforce by 7 employees, representing approximately 58% of the Company’s workforce. The Company estimates it will incur one-time employee related severance expenses of approximately $1.2 million in the first quarter of 2021.

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 Principal Executive Officer and the Company’s Principal Financial and Accounting Officer, 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 Company’s Principal Executive Officer and the Company’s Principal Financial and Accounting Officer, 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, 2020. Based on that evaluation, the Company’s Principal Executive Officer and the Company’s Principal Financial and Accounting Officer conclude whether the Company’s disclosure controls and procedures are effective as of December 31, 2020, at the reasonable assurance level.

In connection with this Annual Report on Form 10-K for the year ended December 31, 2020, an evaluation was performed of the effectiveness of the design and operation of the Company’s disclosure controls and procedures as of December 31, 2020. Based on that evaluation, the Company’s Principal Executive Officer and the Company’s Principal Financial and Accounting Officer have concluded based upon the evaluation described above that, as of December 31, 2020, our disclosure controls and procedures were effective 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, 2020, 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, 2020.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act during the three months ended December 31, 2020 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

/s/ *Joseph Gardner, Ph.D.*
Joseph Gardner, Ph.D.
President and Principal Executive Officer

/s/ *Regina Marek*
Regina Marek
Vice President Finance and Principal Financial and Accounting Officer

March 11, 2021

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The following table sets forth certain information concerning our executive officers and directors as of March 8, 2021.

Name	Age	Position(s)
Executive Officers		
Joseph Gardner, Ph.D.	65	President, Principal Executive Officer
Regina Marek	52	Vice President, Principal Financial and Accounting Officer
Kevin G. Peters, M.D.	64	Chief Scientific Officer and acting Chief Medical Officer
Non-Employee Directors		
Caley Castelein, M.D.	50	Director
Cheryl Cohen	55	Director
Anupam Dalal, M.D.	49	Director
Pravin Dugel, M.D.	57	Director
Steven Prelack	63	Director, Chairman

Executive Officers

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

Regina Marek has served as Aerpio's Vice President of Finance and Principal Financial and Accounting Officer since August 2018. From July 2014 to July 2018, Ms. Marek served as vice president, corporate controller and vice president, integration for Milacron Holdings Corp. From 2012 to 2014, Ms. Marek was vice president of internal audit at Macy's, Inc. and, prior to that she held multiple roles at Owens Corning from 2005 to 2012, including controller of the residential insulation business and director of internal audit for the global composites business. Ms. Marek started her career at Ernst & Young LLP and worked as an auditor and senior manager in the transaction advisory service practice group. Ms. Marek is a licensed and active Certified Public Accountant and received her B.S.B.A in Accounting from John Carroll University and her M.B.A. from Bowling Green State University.

Kevin G. Peters, M.D. has served as Aerpio's Chief Scientific Officer since November 2011 and as acting Chief Medical Officer since May 2019. Dr. Peters guided the development of AKB-9778 and ARP-1536 while at Akebia Therapeutics, Inc., and continues to be in charge of scientific discovery and development for Aerpio. From 2006 to 2010 he served as Group Medical Director of Cardiovascular and Metabolic Disease in Global and Discovery Medicine at Bristol Myers Squibb Co., and from 1998 to 2006 he served as head of Therapeutic Angiogenesis research at P&G Pharmaceuticals Inc. Dr. Peters served as an Associate Professor of Medicine and Pharmacology in the Division of Cardiology at Duke University Medical Center. After receiving his M.D. from the University of Iowa, Dr. Peters completed an internal medicine residency at the University of Minnesota, a clinical fellowship in cardiology at the University of Iowa and a research fellowship as UCSF. He received and B.A. in Biology and Chemistry (double major) Summa Cum Laude from Augustana College.

Board Composition

Non-Employee Directors

Caley Castelein, M.D. has served on Aerpio's board of directors since March 2017. Dr. Castelein is the Founder and has been a Managing Director for Kearny Venture Partners since 2006. Dr. Castelein is also the Founder and has been the Managing Director for KVP Capital since 2013. He is a director for ViewRay, Boreal and Newbridge Pharmaceuticals. Previously, Dr. Castelein served on the board of directors of Alivecor from April 2015 to March 2020. Dr. Castelein received his M.D. from University of California, San Francisco and his A.B. in Biology from Harvard University. We believe that Dr. Castelein is qualified to serve as a director based on his industry experience and service on multiple company boards.

Cheryl Cohen has served on Aerpio's board of directors since June 2018. Ms. Cohen currently serves as president of CLC Consulting, LLC, a pharmaceutical and biotechnology consulting firm specializing in new product start-up and commercialization, which she incorporated in 2008. From 2011 to 2014, Ms. Cohen served as Chief Commercial Officer of Medivation, Inc., where she established and led the company's commercial organization and was responsible for the U.S. launch of Xtandi® (enzalutamide) for metastatic castration-resistant prostate cancer. Ms. Cohen held leadership roles for over a decade at Johnson & Johnson, including as vice president, strategic commercial group, Health Care Systems, Inc., and as vice president, rheumatology franchise, Centocor, Inc. Ms. Cohen began her career at Solvay Pharmaceuticals, Inc. in a variety of sales positions. Since January 2021, Ms. Cohen has served on the boards of directors of Ignyte Acquisition Corp, MEI Pharma, Inc. and NantKwest, Inc. Previously, she served on the boards of directors of CytRx Corporation from June 2015 to October 2016, Eledon Pharmaceuticals, Inc. (previously Novus Therapeutics) from April 2015 to June 2020 and Vital Therapies, Inc. from July 2015 to April 2019. Ms. Cohen received her B.A. from Saint Joseph College. We believe that Ms. Cohen is qualified to serve as director based on her industry experience and service on multiple company boards.

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

Pravin U. Dugel, M.D. has served as a member of Aerpio's board of directors since March 2017. Since April 2020, Dr. Dugel has been the Executive Vice President and Chief Strategy and Business Officer for IVERIC bio, Inc., a publicly traded biopharmaceutical company. Formerly, Dr. Dugel was the Managing Partner of Retinal Consultants of Arizona from 2004 to 2019 and he is a Founding Member of the Spectra Eye Institute. Dr. Dugel is a Clinical Professor at the USC Roski Eye Institute, Keck School of Medicine at the University of Southern California. Dr. Dugel serves on the Advisory Board of Acucela, Inc. and as a member of the Scientific Advisory Board at MacuSight, Inc., Alcon Surgical, Genentech and Novartis. He also serves as a Member of the Medical Advisory Board at TrueVision Systems, Inc. and a Member of the Clinical Advisory Board at Opthea Limited. Dr. Dugel received his M.D. from UCLA School of Medicine and his B.A. from Columbia University. We believe that Dr. Dugel is qualified to serve as a director based on his industry experience and service on multiple boards.

Steven Prelack has served on Aerpio's board of directors since March 2017. Mr. Prelack has been the Chief Operating Officer and Senior Vice President of VetCor, Inc. since 2010. Formerly, he served as a director and audit committee chair at Pieris Pharmaceuticals, Inc. until June 2019 and Galectin Therapeutics Inc. until December 2017. Mr. Prelack is a CPA and has a B.B.A. in Finance and Accounting from the University of Massachusetts, Amherst. We believe that Mr. Prelack is qualified to serve as a director based on his industry experience and service on multiple company boards.

Corporate Governance Guidelines

The Board has adopted corporate governance guidelines to assist and guide its members in the exercise of its responsibilities. These guidelines should be interpreted in accordance with any requirements imposed by applicable federal or state law or regulation and our Amended and Restated Certificate of Incorporation and bylaws. Our corporate governance guidelines are available on our website at www.aerpio.com. Although these corporate governance guidelines have been approved by the Board, it is expected that these guidelines will evolve over time as customary practice and legal requirements change. In particular, those guidelines that encompass legal, regulatory or exchange requirements as they currently exist will be deemed to be modified as and to the extent that such legal, regulatory or exchange requirements are modified. In addition, the guidelines may also be amended by the Board at any time as it deems appropriate.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. 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.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. Our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Anti-Hedging and Anti-Pledging Policies

Our insider trading policies prohibit all directors, executive officers, and certain employees from buying or selling derivatives on our securities, engaging in hedging transactions involving our securities or holding our securities in a margin account, and only allow our securities to be pledged as collateral for a loan with the prior approval by the Audit Committee which must have at least two (2) weeks to consider any such request for approval. To date no such requests have been made or approved.

Board Structure and Committees

Board Composition and Structure

Our Amended and Restated Certificate of Incorporation states that the number of directors shall be fixed exclusively by our Board. Each director holds office until his or her successor is duly elected and qualified or until his or her death, resignation or removal. Our Amended and Restated Certificate of Incorporation provides that our directors may be removed only for cause by the affirmative vote of the holders of at least 66 2/3% of the voting power of the outstanding shares of capital stock of the Company then entitled to vote generally on the election of directors, voting together as a single class, at a meeting of the stockholders called for that purpose. Any vacancy on the Board, including a vacancy that results from an increase in the number of directors, may be filled by a vote of the supermajority (66 2/3%) of the directors then in office, even if less than a quorum.

Our Amended and Restated Certificate of Incorporation provides that our Board is divided into three classes of directors, with the classes as nearly equal in number as possible. Each of our directors previously identified serves in the class indicated. Subject to any earlier resignation or removal in accordance with the terms of our Amended and Restated Certificate of Incorporation and our bylaws each director will serve for a three year period. Our Class I directors will serve until the 2021 annual meeting of stockholders; our Class II directors will serve until the 2022 annual meeting of stockholders; and our Class III directors will serve until the 2023 annual meeting of stockholders. Any additional directorships resulting from an increase in the number of directors will be apportioned by our Board among the three classes.

Director Nomination Process

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

- personal and professional integrity;
- ethics and values;

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

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

Directors Independence

Our securities are listed on the Nasdaq Capital Market which has a requirement that a majority of directors be independent. We evaluate independence by the standards for director independence set forth in the Nasdaq Marketplace Rules. Under such rules, our Board has determined that all members of the Board, except Joseph Gardner, are independent directors. Joseph Gardner is not an independent director under these rules because he is an executive officer of our company. In making such independence determination, our Board considered the relationships that each non-employee director has with us and all other facts and circumstances that our Board deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our Board considered the association of our directors with the holders of more than 5% of our common stock. The composition and functioning of our Board and each of our committees complies with all applicable requirements of the Nasdaq Capital Market and the rules and regulations of the SEC. There are no family relationships among any of our directors or executive officers.

Stockholder Recommendations

Stockholders may submit recommendations for director candidates to the Nominating and Corporate Governance Committee by sending the individual's name and qualifications in writing to our Secretary at Aerpio Pharmaceuticals, Inc., 9987 Carver Road, Suite 420, Cincinnati, Ohio 45242 in accordance with the bylaws of the Company, who will forward all recommendations to the Nominating and Corporate Governance Committee. The Nominating and Corporate Governance Committee will evaluate any candidates recommended by stockholders against the same criteria and pursuant to the same policies and procedures applicable to the evaluation of candidates proposed by directors or management.

Board Leadership Structure and Role of Board in Risk Oversight

Board Leadership Structure

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

Risk Oversight

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations, strategic direction and intellectual property as more fully discussed in the section entitled “Risk Factors” located within this Annual Report on Form 10-K for the fiscal year ended December 31, 2020.

Management is responsible for the day-to-day management of risks we face, while our Board, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our Board has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

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

Board Meetings and Attendance

The Board held 12 meetings during 2020, and each of the incumbent directors of the board attended at least 75% of the aggregate of all meetings of the board and all meetings of committees of our board upon which they served (during the periods that they served) during 2020. The Board regularly holds executive sessions of the independent directors. Executive sessions do not include employee directors or directors who do not qualify as independent under SEC rules. Members of our board are encouraged to attend annual meetings of our stockholders. Seven directors attended the 2020 Annual Meeting of Stockholders.

Board Committees

We have established the following board committees: audit committee, compensation committee and a nominating and corporate governance committee. Each committee operates pursuant to a charter adopted by our Board. The composition and functioning of all committees comply with all applicable requirements of the Sarbanes-Oxley Act of 2002, SEC rules and regulations, and the Nasdaq Capital Market.

The following table sets forth which directors currently serve on each committee of the Board.

Name	Nominating and Corporate Governance	Compensation	Audit
Caley Castelein, M.D.		M	M
Cheryl Cohen	CH		M
Anupam Dalal, M.D.		CH	
Pravin Dugel	M		
Steven Prelack			CH

Audit Committee

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

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;

- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and making recommendations to our Board regarding all such transactions; and
- reviewing quarterly earnings releases.

The Audit Committee held four meetings during 2020. A copy of the Audit Committee Charter is available on the Company's website at *www.aerpio.com* under the Investors section.

Compensation Committee

Anupam Dalal and Caley Castelein serve on the Compensation Committee, which is chaired by Anupam Dalal. Our Board has determined that each member of the Compensation Committee is "independent" as defined in the applicable Nasdaq rules. The Compensation Committee's responsibilities include:

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

The Compensation Committee held no meetings during 2020. A copy of the Compensation Committee Charter is available on the Company's website at *www.aerpio.com* under the Investors section.

<u>Compensation Consultant</u>

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

- trends and emerging topics with respect to executive compensation;
- peer group selection for executive compensation benchmarking;
- compensation practices of our peer group;

- compensation programs for executives and all of our employees; and
- stock utilization and related metrics.

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

In determining to engage Radford, the compensation committee considered the independence of Radford taking into consideration relevant factors, including the absence of other services provided to us by Radford, the amount of fees we paid to Radford as a percentage of Radford's total revenue, the policies and procedures of Radford that are designed to prevent conflicts of interest, any business or personal relationship of the individual compensation advisors employed by Radford with any of our executive officers, any business or personal relationship the individual compensation advisors employed by Radford have with any member of the compensation committee, and any shares of our stock owned by Radford or the individual compensation advisors employed by Radford. The compensation committee has determined, based on its analysis in light of all relevant factors, including the factors listed above, that the work of Radford and the individual compensation advisors employed by Radford as compensation consultants to the compensation committee has not created any conflicts of interest and that Radford is independent pursuant to the independence standards set forth in the Nasdaq Capital Market listing standards promulgated pursuant to Section 10C of the Securities Exchange Act of 1934, as amended (the "Exchange Act").

Nominating and Corporate Governance Committee

Cheryl Cohen and Pravin Dugel currently serve on the Nominating and Corporate Governance Committee, which was chaired by Cheryl Cohen. Our Board has determined that each member of the Nominating and Corporate Governance Committee is "independent" as defined in the applicable Nasdaq rules. The Nominating and Corporate Governance Committee's responsibilities include:

- developing and recommending to the Board criteria for board and committee membership;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the Board to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the Board;
- recommending to the Board the persons to be nominated for election as directors and to each of the Board's committees;
- developing and recommending to the Board a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our Board and management.

The Nominating and Corporate Governance Committee held no meeting during 2020. A copy of the Nominating and Corporate Governance Committee Charter is available on the Company's website at *www.aerpio.com* under the Investors section.

Our Board may from time to time establish other committees.

Item 11. Executive Compensation.

The following summarizes the compensation earned by our executive officers named in the "Summary Compensation Table" below (referred to herein as our "named executive officers") for the year ending December 31, 2020. This section also discusses the material elements of our executive compensation policies and decisions and important factors relevant to an analysis of these policies and decisions. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the information presented in the following tables and the corresponding narrative.

Overview

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

The named executive officers for the year ended December 31, 2020 were as follows:

- Joseph H. Gardner Ph.D., our President, Founder and Principal Executive Officer
- Regina Marek, our Vice President of Finance and Principal Financial and Accounting Officer;
- Kevin G. Peters, M.D., our Chief Scientific Officer and acting Chief Medical Officer

Elements of Executive Compensation

Base Salaries

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

Annual Cash Bonuses

All of the named executive officers participate in the Aerpio Pharmaceuticals, Inc. Senior Executive Cash Incentive Bonus Plan, or the Incentive Plan, which promotes and rewards the executives for the achievement of key strategic and business goals. The 2020 Incentive Plan period covered the 12-month period beginning on January 1, 2020 and ending on December 31, 2020. For the 2020 Incentive Plan period, the target annual bonus as a percentage of base salary, as determined based on the salary earned throughout the bonus plan period, for each of the named executive officers is further described in the section titled "*Executive Compensation—Employment Agreements*." At the beginning of the 2020 bonus plan period, the Compensation Committee established corporate performance goals, each having a designated weighting, which related to key development, strategic and financial goals of our company. At the end of the 2020 bonus plan period, the Compensation Committee met and evaluated the performance of the Company against the specified performance goals. Based on its evaluation, the Compensation Committee recommended, and the Board approved, that we achieved 50% of our corporate goals. Consequently, the Board approved payment of cash bonuses to the named executive officers for the 2020 bonus plan period in the amounts reported in the "Summary Compensation Table—2020" below.

Cash Retention Bonuses

On May 14, 2019, the Board approved cash retention payments to its salaried employees, which were paid at the end of the second quarter in fiscal year 2020. Joseph Gardner, President and principal executive officer, Regina Marek, Vice President Finance and principal financial and accounting officer and Kevin Peters Chief Scientific and acting Chief Medical Officer received cash payments of $210,000 $120,000 and $180,000, respectively. The Board approved payment of cash retention bonuses to the named executive officers in the amounts reported in the "Summary Compensation Table—2020" below.

Equity Awards

The named executive officers have historically participated in Aerpio's 2011 Equity Incentive Plan, or 2011 Plan, and the Stock Option and Incentive Plan, or 2017 Plan.

In March 2020, we made annual equity award grants to each of our named executive officers. We granted Dr. Gardner an option to purchase 155,000 shares of our common stock, Ms. Marek an option to purchase 93,000 shares of our common stock, Dr. Peters an option to purchase 129,000 shares of our common stock each having an exercise price of $0.52 per share, which was the closing price of our stock on the date of grant. These options vest 25% on the first anniversary of the applicable vesting commencement date and then in 36 monthly installments thereafter, in each case subject to the executive continuing to provide services through each such vesting date. These equity awards serve to align the interests of our named executive officers with our stockholders.

We believe that equity grants with a time-based vesting feature promote retention because this feature incentivizes our named executive officers to remain in our employment during the vesting period.

Other Benefits

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

Summary Compensation Table – 2020

The following table sets forth information regarding compensation awarded to, earned by or paid to each of the named executive officers for the years ending December 31, 2020 and 2019.

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)	Bonus ($) (2)	Non-Equity Incentive Compensation ($)(3)	All Other Compensation ($)		Total ($)
Joseph Gardner	2020	432,600	48,427	210,000	108,150	1,646	(4)	590,823
President and Founder, Principal Executive Officer	2019	420,000	510,423	—	199,500	1,069	(4)	1,130,992
Regina Marek	2020	278,100	29,057	120,000	48,668	350	(4)	356,175
VP Finance, Principal Financial and Accounting Officer	2019	244,643	168,866	—	71,708	373	(4)	485,590
Kevin Peters	2020	370,800	40,304	180,000	74,160	1,003	(4)	486,267
Chief Scientific and acting Chief Medical Officer	2019	360,000	450,200	—	136,800	1,069	(4)	948,069

(1) The amounts reported in the Option Awards column represent the grant date fair value of the stock options granted to the named executive officers as of the grant date as computed in accordance with FASB ASC Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in the Option Awards column are set forth in Note 7 to our financial statements for the years ended December 31, 2020 and 2019. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options.

(2) Amounts represent cash retention bonuses paid in 2020.

(3) Amounts represent cash bonuses earned for performance in 2020 and 2019 based upon achievement of corporate performance goals for the respective year.

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

Outstanding Equity Awards at December 31, 2020

The following table sets forth information concerning outstanding equity awards for each of the named executive officers as of December 31, 2020:

	Option Awards					
Name and Principal Position	**Vesting Commencement Date**	**Number of Securities Underlying Unexercised Options (#) Exercisable**	**Number of Securities Underlying Unexercised Options (#) Unexercisable (1)**		**Option Exercise Price ($)**	**Option Expiration Date**
Joseph Gardner	3/16/2020	—	155,000	1	0.52	3/16/2030
President and Founder,	5/14/2019	174,675	174,675	2	1.04	5/14/2029
Principal Executive Officer	2/15/2019	68,750	81,250	1	3.27	2/15/2029
	4/23/2018	100,000	50,000	1	3.59	4/23/2028
	12/14/2017	135,000	—	1	5.50	12/14/2027
	2/18/2014	207,628	—	1	2.11	2/18/2024
	3/22/2012	27,727	—	1	1.66	3/22/2022
Regina Marek	3/16/2020	—	93,000	1	0.52	3/16/2030
VP of Finance, Principal	11/4/2019	20,302	23,998	1	0.5588	11/4/2029
Finance and Accounting Officer	5/14/2019	76,650	76,650	2	1.04	5/14/2029
	2/15/2019	13,750	16,250	1	3.27	2/15/2029
	8/9/2018	46,667	33,333	1	3.49	8/9/2028
Kevin Peters	3/16/2020	—	129,000	1	0.52	3/16/2030
Chief Scientific and acting	5/14/2019	25,031	38,219	1	1.04	5/14/2029
Chief Medical Officer	5/14/2019	133,275	133,275	2	1.04	5/14/2029
	2/15/2019	57,292	67,708	1	3.27	2/15/2029
	4/23/2018	66,667	33,333	1	3.59	4/23/2028
	3/22/2012	1,912	—	1	1.66	3/22/2022

(1) Unless otherwise noted, each option vests 25% on the first anniversary of the vesting commencement date, then vests in 36 equal monthly installments thereafter, such that the option is vested on the fourth anniversary of the vesting commencement date, subject to the holder continuing to provide services to the Company through such vesting date.

(2) Vests 50% on June 30, 2020, then vests 50% on June 30, 2021, subject to the holder continuing to provide services to the Company through such vesting date.

Employment Agreements

We have entered into employment agreements with each of our named executive officers and our other executive officers. Each employment agreement provides for "at will" employment, meaning that either we or the officer may terminate the employment relationship at any time without cause. The material terms of the employment agreements and separation agreements with our 2020 named executive officers are described below. The terms "change of control," "cause" and "good reason" referred to below are defined in the applicable employment agreement or separation agreement.

Executive Employment Agreement with Joseph H. Gardner

Dr. Gardner entered into an employment agreement with us in March 2017, as amended on October 8, 2017, and further amended on January 31, 2021. Pursuant to his employment agreement, Dr. Gardner receives an annual base salary, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus. For 2020, Dr. Gardner's base salary was equal to $432,600, and his target incentive compensation equal to 50% of his base salary. Dr. Gardner is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

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

In lieu of the payments and benefits described in the preceding paragraph, in the event that Dr. Gardner’s employment is terminated by us without cause or Dr. Gardner resigns for good reason, in either case within 15 months following a “change in control”, subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, he will be entitled to receive (i) a lump sum cash payment equal to one and a half (1.5) times the sum of both (x) Dr. Gardner’s then-current base salary (or his base salary in effect immediately prior to the change in control, if higher) and (y) his target annual incentive compensation, (ii) if Dr. Gardner is participating in our group health plan immediately prior to his termination, a monthly cash payment until the earlier of eighteen (18) months following termination or the end of Dr. Gardner’s COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us and (iii) full acceleration of all time-based equity awards held by Dr. Gardner.

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

Executive Employment Agreement with Regina Marek

Ms. Marek entered into an employment agreement with us in November 2019. Pursuant to her employment agreement, Ms. Marek receives an annual base salary, which is subject to annual review and adjustment, and she is eligible to earn an annual cash incentive bonus. For 2020, Ms. Marek’s base salary was equal to $278,100 and her target annual incentive compensation was equal to 35% of her base salary. Ms. Marek is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans.

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

In lieu of the payments and benefits described in the preceding paragraph, in the event that Ms. Marek’s employment is terminated by us without cause or Ms. Marek resigns for good reason, in either case within 15 months following a “change in control”, subject to the execution and effectiveness of a separation agreement, including a general release of claims in our favor, she will be entitled to receive (i) a lump sum cash payment equal to one and a half (1.5) times the sum of both (x) Ms. Marek’s then-current base salary (or her base salary in effect immediately prior to the change in control, if higher) plus (y) Ms. Marek’s target annual incentive compensation (or her target annual incentive compensation in effect immediately prior to the change in control, if larger), (ii) if Ms. Marek is participating in our group health plan immediately prior to her termination, a monthly cash payment until the earlier of eighteen (18) months following termination or the end of Ms. Marek’s COBRA health continuation period in an amount equal to the amount that we would have made to provide health insurance to her had she remained employed with us and (iii) full acceleration of all time-based equity awards held by Ms. Marek.

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

Executive Employment Agreement with Kevin G. Peters, M.D.

Dr. Peters entered into an employment agreement with us in March 2017. Pursuant to his employment agreement, Dr. Peters receives an annual base salary, which is subject to annual review and adjustment, and he is eligible to earn an annual cash incentive bonus. For 2020, Dr. Peters' base salary was equal to $370,800, and his target incentive compensation equal to 40% of his base salary. Dr. Peters is also eligible to participate in the employee benefit plans available to our employees, subject to the terms of those plans. Dr. Peters' employment agreement also provided for certain severance arrangements that were superseded in the terms of his transition services agreement as described below.

Transition Services Agreement with Kevin G. Peters, M.D.

On February 9, 2021, Dr. Peters entered into a transition services agreement with the Company. The transition services agreement provides for Dr. Peters' departure from his positions as Chief Scientific Officer and Chief Medical Officer of the Company, effective as of the Date of Termination (as defined in the transition services agreement). As a result, Dr. Peters will continue to provide transitional services to the Company until the earlier of March 31, 2021 or the last day of the ongoing trial conducted with MTEC designated RESCUE. Under this transition services agreement, Dr. Peters is entitled to receive a continuation of his current base salary, remain eligible to participate in the Company's group employee benefit plans and continue to vest in his outstanding equity awards during this transition period. In connection with the ending of his employment, Dr. Peters will receive his current base salary through the Date of Termination, any unused vacation accrued through the Date of Termination, unpaid expense reimbursements, and any vested benefits under any employee benefit plan through the Date of Termination. Additionally, if Dr. Peters complies with the transition services agreement and satisfies the conditions set forth therein, then following the Date of Termination, Dr. Peters will be entitled to receive (i) monthly cash payments in an amount equal to 12 months of his current base salary, (ii) a monthly cash payment for medical and dental benefits in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us for 12 months or for Dr. Peters' COBRA health continuation period, whichever ends earlier, and (iii) acceleration of vesting on any time-based stock options in which Dr. Peters would have vested if he had remained employed for an additional 12 months. However, in the event that Dr. Peters complies with the transition services agreement and satisfies the conditions set forth therein, and a change in control (as defined in his transition services agreement) occurs prior to his Date of Termination or within three months following the Date of Termination, then in lieu of the severance payments and benefits described in the preceding sentence, Dr. Peters will be entitled to receive: (i) a lump sum in cash in an amount equal to 1.5 times the sum of both Dr. Peters' current base salary (as defined in his transition services agreement) plus his target annual incentive bonus (as defined in his transition services agreement) for the year in which the termination occurs, (ii) a monthly cash payment for medical and dental benefits in an amount equal to the amount that we would have made to provide health insurance to him had he remained employed with us for 18 months or for Dr. Peters' COBRA health continuation period, whichever ends earlier, and (iii) acceleration of vesting on any stock options subject to time-based vesting. This agreement also contains a general release of claims against the Company and a non-disparagement provision.

Retirement Plan

We offer a 401(k) plan to eligible employees, including our named executive officers. In accordance with this plan, all eligible employees may contribute a percentage of compensation up to a maximum of the statutory limits per year. Company contributions are discretionary. We made no contributions during the year ended December 31, 2020. We intend for the 401(k) plan to qualify, depending on the employee's election, under Section 401(a) of the Code, so that contributions by employees, and income earned on those contributions, are not taxable to employees until withdrawn from the 401(k) plan.

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

The following table contains information about our equity compensation plans as of December 31, 2020. As of December 31, 2020, we had three equity compensation plans, each of which was approved by our stockholders: our 2011 Plan, our 2017 Plan and our Amended and Restated 2017 Employee Stock Purchase Plan.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (1)	Weighted average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (1))	
Equity compensation plans approved by security holders (1)	4,642,240	$ 1.81	3,634,905	(2)
Warrants (3)	600,000			
Total	5,242,240		3,634,905	(2)

(1) Includes the following plans: our 2011 Equity Incentive Plan, our 2017 Stock Option and Incentive Plan and our Amended and Restated 2017 Employee Stock Purchase Plan.

(2) Excludes (i) 1,890,052 additional shares of common stock that may be issued pursuant to our 2017 Stock Option and Incentive Plan pursuant to an automatic annual increase effective on January 1, 2021 and (ii) 350,000 additional shares of common stock that may be issued pursuant to our Amended and Restated 2017 Employee Stock Purchase Plan pursuant to an annual increase effective on January 1, 2021.

(3) Warrants issued outside of our equity compensation plans. These warrants have an exercise price of $0.486 and are fully vested.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information relating to the beneficial ownership of our common stock at March 8, 2021 by:

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

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of March 8, 2021 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by such person.

The percentage of shares beneficially owned is computed on the basis of 47,251,319 shares of common stock outstanding as of March 8, 2021. Shares of common stock that a person has the right to acquire within 60 days of March 8, 2021 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed in the table is c/o Aerpio Pharmaceuticals, Inc., 9987 Carver Road, Suite 420, Cincinnati, Ohio 45242.

	Shares Beneficially Owned	
	Number	**Percentage**
5% Stockholders:		
Satter Entities (1)	5,621,835	11.9%
Entities affiliated with OrbiMed Private Investments V, LP(2)	5,193,946	11.0%
The Vanguard Group, Inc. (3)	2,711,579	5.7%
Named Executive Officers and Directors:		
Steven Prelack(4)	42,800	*
Caley Castelein(5)	327,171	*
Cheryl Cohen (6)	54,540	*
Anupam Dalal(7)	49,533	*
Pravin Dugel(8)	66,506	*
Joseph Gardner(9)	1,390,028	2.9%
Kevin Peters(10)	669,671	1.4%
Regina Marek(11)	209,331	*
All directors and executive officers as a group (8 persons) (12)	2,809,580	5.8%

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

(1) Based solely on a Schedule 13D/A filed with the SEC on November 23, 2020, consists of 5,621,835 shares of common stock that are held by Satter Management Co., L.P., for which Muneer A. Satter has sole voting and dispositive power over all such shares. The address of Satter Management Co., L.P. is 676 North Michigan Avenue, Suite 4000, Chicago, Illinois 60611.

(2) Based solely on a Schedule 13D/A filed with the SEC on November 12, 2020, consists of 5,193,946 shares of common stock owned directly by OrbiMed Private Investments V, LP, or OPI V. OrbiMed Capital GP V LLC, or GP V, is the general partner of OPI V. OrbiMed Advisors LLC, or OrbiMed, pursuant to its authority as the managing member of GP V, may be deemed to indirectly beneficially own the Shares held by OPI V. By virtue of such relationships, GP V and OrbiMed may be deemed to have voting and investment power over the shares held by OPI V and as a result may be deemed to have beneficial ownership of such shares. Each of GP V and OrbiMed disclaims beneficial ownership of the shares held by OPI V, except to the extent of its pecuniary interest therein, if any. The address of OrbiMed Investments and OrbiMed Associates is c/o OrbiMed Advisors LLC, 601 Lexington Avenue, 54th Floor, New York, New York 10022.

(3) Based solely on a Schedule 13G filed with the SEC on February 10, 2021, consists of 2,711,579 shares of common stock that are held by The Vanguard Group, Inc. and its subsidiaries listed on Appendix A of Schedule 13G (collectively, "Vanguard"). According to Schedule 13G, Vanguard had the sole power to dispose of 2,698,373 shares of common stock; the shared power to vote 2,964 shares of common stock; and the shared power to dispose of 13,206 shares of common stock. The address of Vanguard is 100 Vanguard Boulevard, Malvern, Pennsylvania 19355.

(4) Consists of 42,800 shares of common stock issuable directly to Steven Prelack upon the conversion of options within 60 days of March 8, 2021.

(5) Consists of (i) 279,907 shares of common stock held directly by Caley Castelein and (ii) 47,264 shares of common stock issuable upon the conversion of options within 60 days of March 8, 2021.

(6) Consists of 54,540 shares of common stock issuable directly to Cheryl Cohen upon the conversion of options within 60 days of March 8, 2021.

(7) Consists of (i) 2,269 shares of common stock held directly by Anupam Dalal and (ii) 47,264 shares of common stock issuable upon the conversion of options within 60 days of March 8, 2021.

(8) Consists of 66,506 shares of common stock issuable directly to Pravin Dugel upon the conversion of options within 60 days of March 8, 2021.

(9) Consists of (i) 453,019 shares of common stock held directly by Joseph Gardner, (ii) 150,000 shares of common stock held in a family trust for the benefit of Dr. Gardner's children and (iii) 787,009 shares of common stock issuable upon the conversion of options within 60 days of March 8, 2021.

(10) Consists of (i) 320,536 shares of common stock held directly by Kevin Peters and (ii) 349,135 shares of common stock issuable upon the conversion of options within 60 days of March 8, 2021.

(11) Consists of (i) 11,625 shares of common stock held directly by Regina Marek and (ii) 197,706 shares of common stock issuable upon the conversion of options within 60 days of March 8, 2021.

(12) Includes an aggregate of 1,592,224 shares issuable upon exercise of stock options within 60 days of March 8, 2021 held by our executive officers and directors as a group.

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

Director Compensation

On March 15, 2017, we adopted a compensation policy for our non-employee directors, or the Director Compensation Program that was designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Pursuant to the Director Compensation Program, our non-employee directors will receive cash compensation, paid quarterly, as follows:

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

Under the Director Compensation Program, upon the director's initial appointment or election to our Board, each non-employee director will receive an option (the Initial Grant) to purchase shares of our common stock with an aggregate grant date fair value (as defined below) equal to $181,400. In addition, each non-employee director who has been serving as a director for the prior three months and will continue to serve as a director immediately following each annual stockholder meeting, will receive, on the date of such annual stockholder meeting, an option (the Annual Grant) to purchase shares of our common stock with an aggregate grant date fair value equal to $90,700. For purposes of the Initial Grant and the Annual Grant, "grant date fair value" will mean the fair value of an award as of the date of grant as determined in accordance with ASC Topic 718, "*Share-Based Payment*", using the Black-Scholes pricing model and the valuation assumptions used by the company in accounting for options as of such date of grant. The Initial Grant will vest as to one-third of the shares subject to Initial Grant on each yearly anniversary of the applicable grant date, subject to continued service through each applicable vesting date, and the Annual Grant will fully vest on the earlier of the first anniversary of the applicable grant date or the date of the next annual stockholder meeting, subject to continued service through such vesting date. In June 2020, the Board deemed it appropriate to reduce the value to be received for the 2020 Annual Grant, we granted to each of our non-employee directors as of the date of the 2020 annual meeting of stockholders a fixed number of options to purchase 52,144 shares of our common stock, with a grant date fair value of $39,672.

2020 Director Compensation Table

The following table sets forth information for the year ended December 31, 2020, regarding the compensation awarded to, earned by or paid to our non-employee directors as of December 31, 2020. Directors who are also our employees receive no additional compensation for their service as a director. The compensation received by Dr. Gardner as an employee of the Company is presented in "*Executive Compensation—Summary Compensation Table—2020*".

Name	Fees Earned or Paid in Cash($)	Option Awards ($)(1)	Total($)
Caley Castelein, M.D. (2)	45,083	39,672	84,755
Cheryl Cohen (3)	48,617	39,672	88,289
Anupam Dalal, M.D. (4)	45,000	39,672	84,672
Pravin U. Dugel, M.D. (5)	36,808	39,672	76,480
Steven Prelack (6)	62,917	39,672	102,589
Muneer Satter (7)	30,692	—	30,692
Chau Khuong (7)	20,300	—	20,300

(1) The amounts reported in the Option Awards column represent the grant date fair value of the stock options granted to our non-employee directors as of the grant date as computed in accordance with FASB ASC Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in the Option Awards column are set forth in Note 7 to our financial statements for the years ended December 31, 2020 and 2019. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by our non-employee directors from the options.

(2) As of December 31, 2020, Dr. Castelein held 94,944 unexercised options.

(3) As of December 31, 2020, Ms. Cohen held 116,344 unexercised options.

(4) As of December 31, 2020, Dr. Dalal held 94,944 unexercised options.

(5) As of December 31, 2020, Dr. Dugel held 114,186 unexercised options,

(6) As of December 31, 2020, Mr. Prelack held 94,944 unexercised options.

(7) Mr. Satter and Mr. Khuong were board members through June 2020. Amount reflects fees paid to each Mr. Satter and Mr. Khuong through the end of their board service period.

Item 14. Principal Accounting Fees and Services.

The following table summarizes the fees of Ernst & Young LLP, our independent registered public accounting firm, for each of the last two fiscal years.

Fee Category:	Year Ended December 31, 2020	Year Ended December 31, 2019
Audit fees	$ 330,154	$ 280,920
Audit-related fees	—	—
Tax fees	23,400	24,096
All other fees	—	—
Total Fees	$ 353,554	$ 305,016

Audit Fees

Consist of aggregate fees for professional services provided in connection with the annual audit of our financial statements, the review of our quarterly condensed financial statements, consultation on accounting matters directly related to the audit, and comfort letters, consents and assistance with and review of documented filed with the SEC.

Tax Fees

Consist of aggregate fees for tax compliance, tax advice and tax planning services including the review and preparation of our federal and state income tax returns.

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 80 of this Annual Report on Form 10-K.

(a)(2) Exhibits.

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The Exhibit Index is incorporated herein by reference.

Exhibit Index

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
3.2	Amended and Restated By-laws of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.3 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
4.1	Specimen Stock Certificate evidencing shares of common stock (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 filed with the Securities and Exchange Commission on April 14, 2017, File No. 333-217320)
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 on March 17, 2017, File No. 000-53057)
4.3	Description of Registrant's Securities (incorporated by reference to Exhibit 4.3 to the Registrant's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 16, 2020, File No. 001-38560)
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 Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 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 Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.3#	Amended and Restated 2017 Employee Stock Purchase Plan (incorporated herein by reference to Exhibit 10.1 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on December 18, 2017, File No. 000-53057)
10.4#	Form of Indemnification Agreement (incorporated herein by reference to Exhibit 10.4 to the Registrant's Form 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 Registrant's Form 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 Registrant and the investors party thereto (incorporated herein by reference to Exhibit 10.6 to the Registrant's Form 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 Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057)
10.8	Fourth Amendment to Office Lease and Assignment and Assumption of Lease dated as of March 29, 2018 by and between Blue Ash Landings Acquisition, LLC and Aerpio (incorporated herein by reference to Exhibit 10.1 to the Company's 8-K filed with the Securities and Exchange Commission on April 2, 2018, File No. 000-53057))
10.9	License Agreement dated June 24, 2018, by and between the Registrant and Gossamer Bio, Inc. (incorporated herein by reference to Exhibit 10.1 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on June 25, 2018 (File No. 000-53057))

10.10#	Employment Agreement, dated March 15, 2017, between the Registrant and Joseph H. Gardner (incorporated herein by reference to Exhibit 10.8 to the Registrant'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, dated as of March 15, 2017, between the Registrant and Kevin G. Peters (incorporated herein by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1 filed with the Securities and Exchange Commission on April 14, 2017, File No. 333-217320)
10.12	First Amendment to Employment Agreement, dated October 8, 2017, by and between the Registrant and Joseph Gardner (incorporated herein by reference to Exhibit 10.2 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on October 10, 2017, File No. 000-53057)
10.13	Registration Rights Agreement by and among the Registrant and certain former stockholders of Aerpio (incorporated herein by reference to Exhibit 10.9 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on March 17, 2017, File No. 000-53057).
10.14	Senior Cash Incentive Bonus Plan of the Registrant (incorporated herein by reference to Exhibit 10.15 to the Registrant's Annual Report on Form 10-K filed with Securities and Exchange Commission on March 15, 2018, File No. 000-53057).
10.15#	Form of Inducement Stock Option Award (incorporated herein by reference to Exhibit 99.1 to the Registrant's Form S-8 filed with the Securities and Exchange Commission on December 28, 2018 (File No. 333-229089)
10.16#	Employment Agreement, effective as of November 6, 2019, by and between the Registrant and Regina Marek (incorporated herein by reference to Exhibit 10.1 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on November 7, 2019, File No. 001-38560)
10.17#	Second Amendment to Employment Agreement dated January 31, 2021, by and between Registrant and Joseph Gardner (incorporated herein by reference to Exhibit 10.1 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on February 1, 2021, File No. 001-38560)
10.18#	Transitional Services and Separation Agreement, dated February 9, 2021, by and between the Registrant and Kevin G. Peters (incorporated herein by reference to Exhibit 10.1 to the Registrant's Form 8-K filed with the Securities and Exchange Commission on February 16, 2021, File No. 001-38560)
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 the exhibit is being furnished, not filed, with this report
\# 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 11, 2021

By: */s/ Joseph Gardner, Ph.D.*
Joseph Gardner, Ph.D.
President 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/ Joseph Gardner, Ph.D **Joseph Gardner, Ph.D.**	President, Founder and Director Principal Executive Officer	March 11, 2021
/s/ Regina Marek **Regina Marek**	Vice President Finance and Principal Financial and Accounting Officer	March 11, 2021
/s/ Steven Prelack **Steven Prelack**	Chairman	March 11, 2021
/s/ Cheryl Cohen **Cheryl Cohen**	Director	March 11, 2021
/s/ Caley Castelein, M.D. **Caley Castelein**	Director	March 11, 2021
/s/ Anupam Dalal, M.D. **Anupam Dalal**	Director	March 11, 2021
/s/ Pravin Dugel, M.D. **Pravin Dugel**	Director	March 11, 2021

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) of Aerpio Pharmaceuticals, Inc., 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,
2) Registration Statement (Form S-3 No. 333-223113) of Aerpio Pharmaceuticals, Inc., for the registration of common stock, preferred stock, debt securities, warrants, and/or units,
3) Registration Statement (Form S-8 No. 333-224189) of Aerpio Pharmaceuticals, Inc., 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,
4) Registration Statement (Form S-3 No. 333-217320) of Aerpio Pharmaceuticals, Inc., for the registration of common stock,
5) Registration Statement (Form S-3 No. 333-229087) of Aerpio Pharmaceuticals Inc., for the registration of common stock,
6) Registration Statement (Form S-8 No. 333-229089) of Aerpio Pharmaceuticals, Inc., pertaining to the Inducement Stock Option Agreements,
7) Registration Statement (Form S-8 No. 333-230114) of Aerpio Pharmaceuticals, Inc., pertaining to the Aerpio Pharmaceuticals, Inc. 2017 Stock Option and Incentive Plan and Aerpio Pharmaceuticals, Inc. Amended and Restated 2017 Employee Stock Purchase Plan,
8) Registration Statement (Form S-8 No. 333-237210) of Aerpio Pharmaceuticals, Inc. pertaining to the Aerpio Pharmaceuticals, Inc. 2017 Stock Option and Incentive Plan and Aerpio Pharmaceuticals, Inc. Amended and Restated 2017 Employee Stock Purchase Plan, and

of our report dated March 11, 2021, with respect to the consolidated financial statements of Aerpio Pharmaceuticals, Inc., included in this Annual Report (Form 10-K) of Aerpio Pharmaceuticals, Inc. for the year ended December 31, 2020.

/s/ Ernst & Young LLP

Cincinnati, Ohio
March 11, 2021

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, Joseph Gardner, 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) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (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 11, 2021

By: *\/s/ Joseph Gardner, Ph.D.*

Joseph Gardner, Ph.D.

President and 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, Regina Marek, 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) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) 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) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

    (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 11, 2021

By: */s/ Regina Marek*
Regina Marek
Vice President, Finance and Principal Financial and 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, 2020 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 11, 2021	By: *[/s/ Joseph Gardner, Ph.D.]*
	Joseph Gardner, Ph.D.
	President and 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, 2020 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 11, 2021	By: */s/ Regina Marek*
	Regina Marek
	Vice President, Finance and Principal Financial and Accounting Officer