UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2017

or

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

For the transition period from _____ to _____

Commission File Number: 001-36579

Adverum Biotechnologies, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**20-5258327**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

1035 O'Brien Drive
Menlo Park, California 94025
(650) 272-6269
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.0001 per share	**Nasdaq Global Market**

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

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or 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. (Check one):

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

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

As of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $87.8 million, based on the closing price of the registrant's common stock on the Nasdaq Global Market on June 30, 2017 of $2.50 per share. Shares of the registrant's common stock held by each officer and director and each person known to the registrant to own 10% or more of the outstanding common stock of the registrant have been excluded in that such persons may be deemed affiliates. This determination of affiliate status is not a determination for other purposes.

As of February 28, 2018, the registrant had 62,173,278 shares of common stock, par value $0.0001 par value, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive proxy statement (the Proxy Statement) for the 2018 Annual Meeting of Stockholders of the registrant are incorporated by reference into Part III of this Annual Report on Form 10-K. The Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2017.

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In this report, unless otherwise stated or the context otherwise indicates, references to "Adverum," "Adverum Biotechnologies," "the Company," "we," "us," "our" and similar references refer to Adverum Biotechnologies, Inc., a Delaware corporation.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "could," "will," "would," "should," "expect," "plan," "anticipate," "believe," "estimate," "intend," "predict," "seek," "contemplate," "potential" or "continue" or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, progress, timing, costs and results of preclinical studies and any clinical trials for our product candidates;
- our ability to advance our viral vector manufacturing and delivery capabilities;
- the timing or likelihood of regulatory filings, designations and approvals;
- our plans to explore potential applications of our gene therapy platform in other indications in ophthalmology and rare diseases;
- our expectations regarding the clinical effectiveness of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- our expectation regarding the potential market sizes for our product candidates;
- our intellectual property position;
- the potential benefits of our strategic collaborations and our ability to enter into strategic arrangements;
- developments and projections relating to our competitors and our industry;
- our expectations regarding the time during which we will be an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; and
- the safety, efficacy and projected development timeline and commercial potential of any product candidates.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the heading "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

Any forward-looking statement in this Annual Report on Form 10-K reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this Annual Report on Form 10-K may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

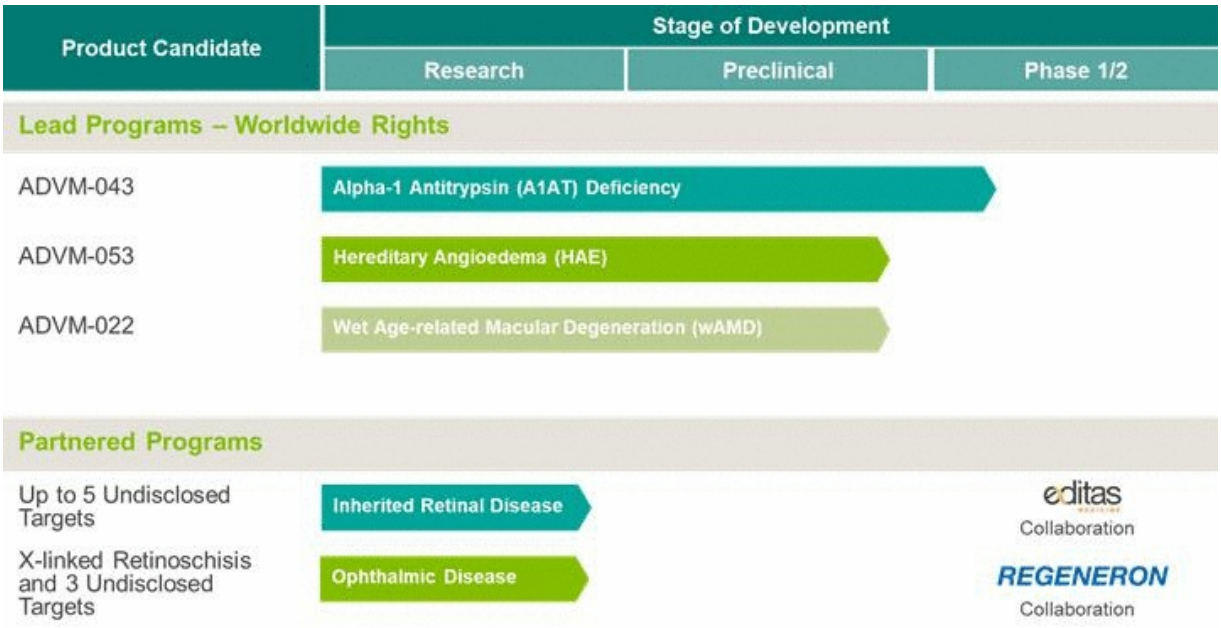
PART 1.

Item 1. Business

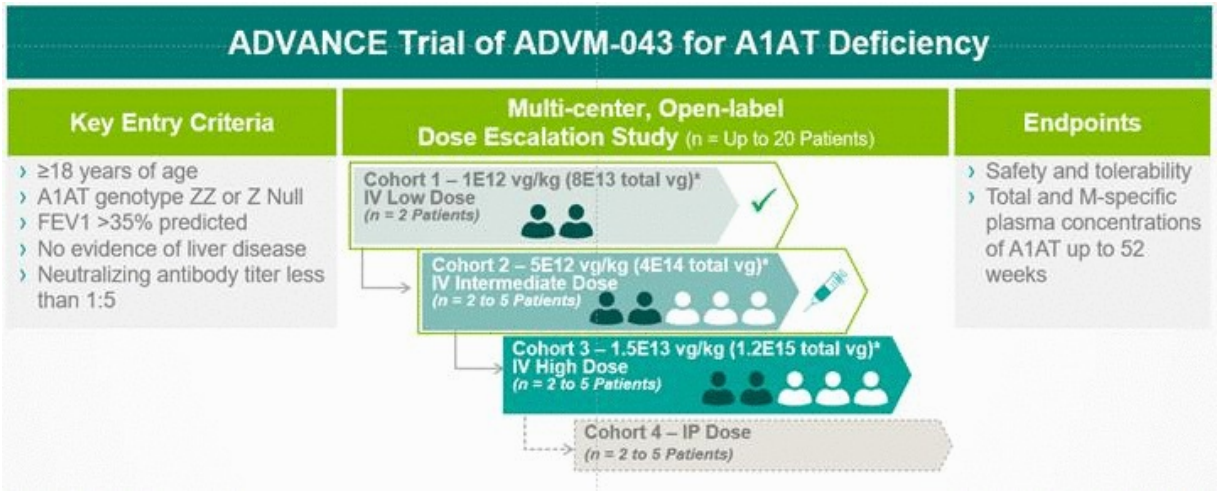
Overview

We are a clinical-stage gene therapy company targeting unmet medical needs in serious rare and ocular diseases. Leveraging our next-generation adeno-associated virus ("AAV")-based directed evolution platform, we generate gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. Our core capabilities include clinical development and in-house manufacturing expertise, specifically in process development, assay development, and current Good Manufacturing Practices ("cGMP") quality control. Our leadership team has significant drug development and gene therapy expertise.

We are advancing our robust pipeline of gene therapy product candidates designed to treat rare diseases, alpha-1 antitrypsin ("A1AT") deficiency and hereditary angioedema ("HAE"), as well as wet age-related macular degeneration ("wAMD"). Our pipeline of lead and partnered gene therapy programs is shown below.



For the treatment of A1AT deficiency, we are advancing our gene therapy product candidate ADVM-043, AAVrh.10-A1AT, in an ongoing Phase 1/2 clinical trial (the "ADVANCE trial"). The ADVANCE trial is a multi-center, open-label, dose-escalation study. The primary endpoint is safety and tolerability and secondary endpoints include changes in plasma concentrations of both total and M-specific A1AT levels. The study will include up to 20 patients across up to four planned dosing cohorts of up to 5 patients each. The first three cohorts of patients will receive a single intravenous ("IV") administration of ADVM-043 and the fourth cohort of patients will receive a single intrapleural ("IP") administration of ADVM-043. In the first cohort, patients (n=2) have been dosed and evaluated following a single administration of ADVM-043 at a dose of ~1E12 vg/kg (8E13 total vg). Based on a review of the preliminary safety data, the independent data monitoring committee ("DMC") has recommended escalating to the intermediate dose (~5E12 vg/kg (4E14 total vg) of ADVM-043, which will be utilized in the second cohort of patients, which is open for enrollment. Further details about the study can be found at ClinicalTrials.gov under trial identifier number NCT02168686. We expect to report preliminary data from this trial in the second half of 2018.



* Based on an 80kg patient

ADVM-043 is designed as a potential single-administration treatment to induce stable, long-term A1AT protein levels, or expression. In a preclinical proof-of-concept study, ADVM-043 demonstrated robust protein expression above therapeutic levels in mice following either IV or IP administration. In another study in non-human primates, evidence of stable long-term expression of hA1AT was observed out to one year following IP administration of ADVM-043.

For treatment of the rare disease HAE, we are advancing our preclinical gene therapy product candidate ADVM-053, AAVrh.10-C1EI. ADVM-053 is designed as a potential single-administration treatment to provide sustained expression of the C1 esterase inhibitor ("C1EI") protein to eliminate protein level variability and to prevent breakthrough edema attacks. In preclinical studies, a single IV administration of ADVM-053 increased C1EI protein expression above therapeutic levels and decreased vascular permeability. We plan to submit an Investigational New Drug ("IND") application for ADVM-053 for HAE with the U.S. Food and Drug Administration ("FDA") in the second half of 2018.

For wAMD, we are advancing our preclinical gene therapy product candidate ADVM-022, AAV.7m8-aflibercept. Comprising a proprietary vector capsid ("AAV.7m8") and a proprietary expression cassette, ADVM-022 is administered as a single intravitreal injection and is designed to minimize the treatment burden of anti-Vascular Endothelial Growth Factor ("VEGF") injections, which is the current standard of care for treatment of wAMD. We have presented preclinical proof-of-concept data of ADVM-022's anti-angiogenic effect in the laser-induced choroidal neovascularization ("CNV") model in non-human primates ("NHP"), the industry standard for testing new wAMD therapies. The data from a single injection of ADVM-022 showed efficacy that was comparable to the anti-VEGF standard of care, which was used as positive control in the CNV study. At scientific meetings in September 2017, we presented additional long-term data, which continued to demonstrate sustained expression of anti-VEGF protein following a single intravitreal injection of ADVM-022. Pharmacokinetic data on one non-human primate demonstrated sustained expression for 52 weeks. In a separate ongoing study, sustained expression for at least seven months has been observed in seven non-human primates. In this ongoing preclinical study, we continue to assess the durability of protein expression in non-human primates and expect to report 12-month efficacy data in the NHP CNV model in the first half of 2018. We plan to submit an IND application for ADVM-022 for wAMD with the FDA in the second half of 2018.

Our earlier-stage research programs include gene therapy product candidates targeting cardiomyopathy associated with Friedreich's ataxia ("FA") and severe allergy.

Our partnered programs include vectors we are developing under collaboration agreements. Under an agreement with Editas Medicine, Inc. ("Editas") we are leveraging our AAV-vectors for use with Editas' leading Clustered Regularly Interspaced Short Palindromic Repeats ("CRISPR")-based genome editing technologies to treat up to five inherited retinal diseases. Our agreement with Regeneron Pharmaceuticals, Inc. ("Regeneron") provides for development of up to eight distinct ocular therapeutic targets, and includes AVA-311 for the treatment of juvenile X-Linked Retinoschisis ("XLRS").

On May 11, 2016, we completed the acquisition of all of the outstanding shares of Annapurna Therapeutics SAS ("Annapurna"), a privately-held French gene therapy company, (the "Annapurna acquisition") and, as a result, Annapurna became our wholly-owned subsidiary. At the closing of the Annapurna acquisition, we issued 14,087,246 shares of our common stock to the shareholders of Annapurna, and the outstanding stock options or other rights to purchase capital stock of Annapurna were exchanged for our stock options or other rights to purchase capital stock of our common stock.

We changed our name from "Avalanche Biotechnologies, Inc." to "Adverum Biotechnologies, Inc." upon completion of the Annapurna acquisition.

Our Strengths

We believe we have the capabilities, resources, and expertise to enable Adverum to become a leading gene therapy company. These strengths include:

- industry-leading capabilities in AAV technology;
- a robust pipeline of gene therapy product candidates targeting the treatment of serious rare and ocular diseases;
- a robust patent portfolio;
- proprietary vectors; and
- an experienced leadership team with expertise in developing gene therapies.

Our Strategy

Our goal is to discover, develop, and commercialize novel gene therapies with the potential to treat patients living with serious rare diseases or diseases of the eye. The key elements of our strategy to achieve this goal are to:

- **Target large patient populations impacted by wAMD and well-established orphan indications offering significant market potential.** For wAMD, there are an estimated 1.2 million individuals in the U.S. and 3 million on a worldwide basis living with this disease, and the incidence of new cases is expected to continue to grow significantly from an aging population. The standard-of-care therapies generated approximately $9.2 billion in sales in 2017. For A1AT deficiency, approximately 100,000 individuals in the U.S. are affected. The therapeutic market for patients with A1AT deficiency was estimated at approximately $575 million in the U.S., $700 million in North America, and $1.2 billion worldwide in 2016. For HAE, there are approximately 8,000 individuals in the U.S. impacted by this disease. The therapeutic market for HAE was approximately $1.7 billion worldwide in 2016.
- **Address unmet needs in serious rare and ocular diseases.** Our gene therapies are designed as single-administration treatments to address the unmet needs of patients with serious rare and ocular diseases. Currently, patients living with A1AT deficiency, HAE and wAMD are treated with therapies that require frequent IV, subcutaneous injection ("SQ"), or intravitreal administration and have significant limitations. As an example, for patients with emphysema due to A1AT deficiency, the current standard-of-care treatment is weekly IV infusions of A1AT. This treatment regimen can be difficult for patients to comply with and underdosing can lead to worsening lung function. For HAE, the current standard-of-care treatment is IV or SQ infusions of C1EI 2-3 times a week, which offer limited efficacy as patients can still have breakthrough attacks, which can be fatal. For wAMD, the current standard-of-care treatment requires patients to receive intravitreal injections of anti-VEGF proteins every 4-8 weeks, which can be difficult for patients to comply with and leads to loss of vision from underdosing.
- **Pursue indications with well-defined clinical and regulatory paths to mitigate the risk of the development of our novel gene therapies.** We have selected indications that have prior clinical validation, including established endpoints, and defined regulatory paths. For example, in A1AT deficiency, published clinical data demonstrate the correlation of patients' serum A1AT protein levels with the risk for emphysema, and four plasma derived protein products have been approved by the FDA based on demonstrating an increase in the A1AT protein levels. Similarly, data show that augmenting serum A1AT protein levels can slow the loss of lung parenchyma. In HAE, there are several therapies approved for routine prophylaxis on the basis of reducing breakthrough attacks by elevating C1-esterase inhibitor levels to an established threshold. For wAMD, anti-VEGF proteins are the approved standard-of-care, and our gene therapy utilizes a proprietary vector designed to deliver an anti-VEGF protein through an intravitreal injection.
- **Accelerate the clinical development of our pipeline of gene therapies toward near-term milestones.** To accelerate the development of our pipeline, we are executing our clinical and regulatory plans to have three gene therapy programs in the clinic in the near term. We are advancing ADVM-043 for the treatment of patients with A1AT deficiency in the ADVANCE trial, which began patient dosing in December 2017. We expect to report preliminary data from the ADVANCE trial in the second half of 2018. For ADVM-022 for wAMD, we are conducting IND-enabling studies as well as an ongoing preclinical study to assess the durability of protein expression in non-human primates and long-term efficacy of ADVM-022 in the laser induced CNV model in NHPs. We expect to report the 12-month efficacy data in the first half of

2018. In addition, we plan to submit an IND application for ADVM 022 for wAMD with the FDA in the second half of 2018. For ADVM-053 for HAE, IND-enabling studies are ongoing and we also plan to submit an IND application with the FDA in the second half of 2018.

- **Advance our earlier-stage research initiatives and leverage our industry-leading capabilities in novel vector development.** We plan to continue to leverage our next-generation AAV-based directed evolution platform to engineer AAV capsid and discover novel vectors with potential enhanced tropism for certain tissues and/or improved antibody neutralization profile over currently existing AAV variants. Combining our vectorology and manufacturing expertise, we have the capability to generate large amounts of high-throughput recombinant AAV capsid libraries that can be screened in large animals rather than rodents in order to maximize chances of applicability to human subjects. We are also focused on discovering improved ubiquitous and cell-specific promoters and expression cassettes to offer optimal transgene expression target tissue. We plan to use this expertise to expand our pipeline and manage and potentially extend the life cycle of our novel gene therapies.
- **Collaborate with partners to leverage our industry-leading AAV vector expertise and ophthalmic vector development and product delivery capabilities.** Under a collaboration agreement with Editas Medicine, we are leveraging our proprietary AAV vectors for use with Editas' leading CRISPR-based genome editing technologies to treat up to five inherited retinal diseases. Our collaboration agreement with Regeneron provides for the development of up to eight distinct ocular therapeutic targets and, includes AVA-311 for the treatment of juvenile XLRS. We plan to continue to explore ways to work collaboratively with these and potential new partners who may benefit from our capabilities and expertise in AAV vector development and product delivery.
- **Prepare manufacturing capabilities for late-stage clinical trials and commercialization.** We plan to begin the initial stage of investing in a manufacturing facility to build on our internal process development capabilities. Our in-house manufacturing process is based on the Baculovirus/Sf9 production system, which has been used for a number of FDA and EMA-approved products and is capable of producing large quantities of AAVs. Currently, we utilize our process development capabilities to deliver scalable processes to GMP contract manufacturers. As we prepare for larger, late-stage clinical trials and potential commercialization, we plan to invest in stages in a manufacturing facility to meet our product production requirements.

Gene Therapy Background

Gene therapy is a powerful treatment modality to address disease biology in a targeted and efficient way. With gene therapy, affected individuals are administered vectors encoding therapeutic genes, expressing for example the functional version of a mutated protein (e.g., A1AT or C1EI) or a therapeutic protein (e.g. anti-VEGF). Instead of providing proteins or other therapies externally and dosing them over a long period, gene therapy offers the possibility of dosing once, or a very limited number of times, to achieve a long-term, durable benefit. Once a patient's cells have incorporated the therapeutic gene, the cells are potentially able to continue to produce the therapeutic protein for years.

Similar to existing classes of protein or biologic therapies such as monoclonal antibodies and drug-antibody conjugates, gene therapy has taken a number of years to evolve from a research tool into a viable and compelling treatment modality. There have been several recent advances in gene therapy, including the following:

- **Compelling clinical data.** Positive data from gene therapy clinical trials have been reported in a variety of indications, including adrenoleukodystrophy, beta-thalassemia, chronic lymphoid leukemia, hemophilia, Spinal Muscular Atrophy, HIV infection and Parkinson's disease, as well as several ophthalmic diseases including biallelic RPE65 mutation-associated retinal dystrophy, Choroideremia and Leber's Hereditary Optic Neuropathy.
- **Increased investment by biopharmaceutical companies.** The modality of gene therapy has been further validated by growing interest and investments by biopharmaceutical companies. Large, global biopharmaceutical companies, such as BioMarin Pharmaceutical Inc., Biogen Idec Inc., Celgene Corporation, GlaxoSmithKline plc, Novartis, Sanofi, Regeneron and Shire Pharmaceuticals Group Plc, have increased their investment in the gene therapy field. Additionally, pure-play gene therapy companies, such as Applied Genetic Technologies Corporation, Audentes Therapeutics, Inc., bluebird bio, Inc., REGENXBIO Inc. ("REGENXBIO"), Spark Therapeutics, Inc., uniQure N.V. and Voyager Therapeutics, have attracted recent investment in this growing field.
- **Approval of gene therapy products by regulatory authorities.** The FDA recently approved its first AAV vector-based gene therapy product, LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

Our Novel AAV Vector Discovery and Optimization System

Our next-generation discovery platform is based on vectors derived from AAV, which is a small, non-pathogenic virus, encoding a therapeutic DNA instead of the viral protein genes. The resulting vector is used to deliver a functional gene into a desired cell population, which when expressed, will result in continuous protein production. We believe AAV vectors offer numerous advantages over other viral and non-viral vector technologies used for gene therapy. These advantages, highlighted below, have the potential to allow AAVs to be safe, to be applicable for a variety of indications and to exhibit long-term efficacy.

- **Highly-efficient transfer of DNA.** AAV vectors offer highly-efficient transfer of DNA to the patient.
- **Non-pathogenic.** Parental AAV virus is not known to cause any disease in humans.
- **Non-replicating.** Parental AAV virus is naturally replication deficient. Once inside the host cell, AAV vectors do not replicate, and cannot spread.
- **Long-term expression.** Once incorporated into the host cell, AAV vectors can continue to drive expression of a therapeutic protein for years. This may avoid the need for frequent treatments, that are the standard of care for the treatment of A1AT deficiency, HAE and wAMD.
- **Low-integrating potential.** AAV vector genomes remain mainly as a stable non-integrated episome in the host cell nucleus, mitigating the risk of potential safety concerns.
- **Low inflammatory potential.** Compared to other vectors used in direct gene therapy approaches, AAV vectors elicit only mild inflammatory reactions.
- **Ability to transduce non-dividing cells.** AAV vectors are able to efficiently transduce non-dividing cells or slow-dividing cells such as retinal cells and hepatocytes which allow production of the therapeutic protein at the site of the disease (wAMD) or its natural organ of production (A1AT).
- **Tested in humans.** AAV vectors have been used safely in more than 130 gene therapy trials to date.

AAV is naturally occurring and has become a leading vector used in gene therapy. According to the *Journal of Gene Medicine*, AAV has been used in over 130 clinical trials as of August 2016. The most frequently studied variant of AAV is AAV2, which can preferentially infect a number of cell types, including those found in the retina.

As effective as existing AAV vectors are in gene therapy, we believe there is an opportunity to advance vector capabilities beyond those currently available. Naturally occurring AAV variants have evolved with particular characteristics, some of which pose limitations to their use in gene therapy.

In order to create next-generation vectors, we use a multi-step process known as directed evolution. Our directed evolution technology uses a library of engineered AAV capsid genes, which exhibit different properties and capabilities than naturally occurring AAVs. Once we have created an initial pool of millions of different AAVs, each with distinct genetic and chemical composition, we screen the AAVs in the pool for novel properties, e.g., specific transduction of a particular cell type of interest or the capability to evade pre-existing neutralizing immune response. After isolating engineered capsids with potentially desirable properties from the target tissue, a smaller pool of optimized vectors from this screening process is further generated and screened until we have identified a select number of engineered AAVs with the characteristics we seek.

Our Product Candidates

We have a pipeline of gene therapy product candidates in development for the treatment of patients with serious rare and ocular diseases.

ADVM-043 for Treatment of A1AT Deficiency

Market for A1AT Deficiency

A1AT deficiency is an orphan disease affecting approximately 100,000 individuals in the United States (the "U.S."). The disease is caused by mutations in the SERPINA1 gene, resulting in very low levels of A1AT. A1AT deficiency is associated with the development of emphysema and premature death.

The market for A1AT deficiency therapy was approximately $575 million in the U.S., $700 million in North America and $1.2 billion worldwide in 2016. The current standard-of-care treatment for patients with this disease who have developed emphysema includes weekly IV infusions of a plasma derived A1AT, at an estimated cost of $100,000 annually per patient. This current treatment regimen is burdensome and can result in underdosing, which in turn can lead to worsening lung function.

Our Approach for A1AT Deficiency

ADVM-043 is our gene therapy candidate that has the potential to induce stable, long-term A1AT protein expression. In a preclinical proof-of-concept study, ADVM-043 demonstrated robust protein expression in mice, with protein levels 2.5 times above normal levels of A1AT. Data showed that hA1AT was present in the serum following either IV or IP administration of ADVM-043. In another study in non-human primates, evidence of stable long-term expression of hA1AT was observed out to one year following IP administration of ADVM-043.

ADVM-043 utilizes AAVrh.10, a vector selected based on peer-reviewed published research which compared 25 different vectors used in the lung showing superiority of protein expression from AAVrh.10 over other serotypes. In addition, AAVrh.10 has been shown to transduce the liver, which is the organ that naturally produces A1AT with high efficiency. Our biodistribution and preclinical data on this vector lead us to believe there is potential for AAVrh.10-A1AT, when administered intravenously, to provide therapeutic levels of A1AT.

We are advancing ADVM-043 in the ADVANCE trial in A1AT deficiency patients and we expect to report preliminary data from this trial in the second half of 2018.

ADVM-053 for Treatment of HAE

Market for HAE

HAE is an orphan disease affecting approximately 8,000 individuals in the U.S. This disease is caused by a genetic mutation that results in low levels of C1EI. Low C1EI levels can be associated with sudden swelling and edema of respiratory airways, gastrointestinal tract, and extremities.

The current standard-of-care prophylaxis treatment regimen generally requires IV infusions or subcutaneous injections of C1EI 2-3 times a week, at an estimated cost of $0.5 million – $0.6 million annually per patient in the U.S. This treatment regimen can be burdensome for patients and their caregivers, and patients may still experience breakthrough edema attacks despite treatment.

A prior study demonstrated that patients treated with more frequent infusions of C1EI can significantly decrease and, in some patients, eliminate breakthrough attacks. However, a daily infusion treatment regimen is not clinically practical and, therefore, there is an unmet medical need for sustained C1EI delivery to patients in order to prevent breakthrough edema attacks.

Our Approach for HAE

ADVM-053 is our preclinical gene therapy product candidate that has the potential to be a prophylactic treatment of HAE. ADVM-053 is designed to be administered as a single IV injection to prevent HAE attacks.

ADVM-053 also utilizes an AAVrh.10-based vector, which has been shown to target the liver, which is the natural source of C1EI. In prior preclinical studies, a single IV administration of ADVM-053 showed robust C1EI protein expression. In a proof-of-concept study, ADVM-053 increased C1EI protein expression above anticipated therapeutic levels. An additional study, in a mouse model of the disease, demonstrated that ADVM-053 decreased vascular permeability.

We are advancing ADVM-053 for HAE and plan to submit an IND with the FDA in the second half of 2018.

ADVM-022 for Treatment of wAMD

Market for wAMD

Age-related macular degeneration ("AMD") is a progressive disease affecting the retinal cells in the macula, the region of the eye responsible for central vision. Disease progression results in the death of retinal cells and the gradual loss of vision.

Approximately 10% of patients living with AMD have an advanced form of the disease called wAMD, in which blood vessels begin to invade the cellular space between layers of cells in the retina. These new blood vessels are often leaky, which results in fluid and blood in the retina and causes vision loss.

wAMD is a leading cause of vision loss in subjects over 60 years of age. A significant number of individuals are impacted by this disease, which has a prevalence of approximately 1.2 million individuals in the U.S. and 3 million on a worldwide basis. The incidence of new cases of wAMD in the U.S. is approximately 150,000 to 200,000 annually, and this number is expected to grow significantly based on the country's aging population.

Although the underlying molecular causes of AMD are not completely known, VEGF is known to play a central role in the growth of new blood vessels in wAMD. The standard-of-care therapies for wAMD include Lucentis® and EYLEA®, which together generated annual sales of approximately $9.2 billion in 2017, in addition to off-label use of Avastin®.

- Lucentis, a recombinant humanized monoclonal antibody fragment that binds to and inhibits VEGF proteins in the eye, was approved in the U.S. in 2006 and in Europe in 2007. In 2017, Lucentis achieved worldwide sales of approximately $3.3 billion.
- EYLEA, a recombinant fusion protein containing portions of the human VEGF receptors that binds to VEGF, was approved in the U.S. in 2011. EYLEA has exhibited strong adoption in the market due to its more convenient dosing regimen compared to Lucentis and in 2017, EYLEA® achieved worldwide sales of approximately $5.9 billion.
- Avastin is a recombinant human monoclonal antibody that binds to VEGF and is approved as an anti-cancer agent. Avastin is widely prescribed off-label in ophthalmic diseases such as wAMD and makes up approximately 60% of the wAMD market by volume.

The current treatment regimen can be burdensome, as patients generally require intravitreal injections with anti-VEGF proteins every 4-8 weeks. Compliance with this regimen can be difficult for patients and their caregivers, leading to compliance deficiencies and loss of vision from underdosing.

Our Approach for wAMD

ADVM-022 is our preclinical gene therapy product candidate for the treatment of wAMD. With AAV.7m8 and a proprietary expression cassette, ADVM-022 is administered as a single intravitreal injection and is designed to minimize the treatment burden of the standard of care frequent injections. At scientific meetings, we have presented preclinical proof-of-concept data of ADVM-022's anti-angiogenic effect in the laser-induced CNV model in non-human primates, the industry standard for testing new wAMD therapies. The data from a single injection of ADVM-022 showed efficacy that was comparable to the anti-VEGF standard of care, which was the positive control in the CNV model. We presented additional long-term data at scientific meetings in September 2017, which continued to demonstrate sustained expression of anti-VEGF protein following a single intravitreal injection of ADVM-022. Pharmacokinetic data on one non-human primate demonstrated sustained expression for 52 weeks. In a separate ongoing study, sustained expression for at least seven months has been observed in seven non-human primates. In this ongoing preclinical study, we continue to assess the durability of protein expression in non-human primates and expect to report 12-month efficacy data for ADVM-022 in the laser induced CNV model in the first half of 2018.

We are advancing ADVM-022 and plan to submit an IND application with the FDA in the second half of 2018.

GenSight Biologics has also obtained a license from us to use AAV.7m8 for GS030 gene therapy encoding channelrhodopsin protein. GenSight has received MHRA approval to initiate a Phase 1/2 trial in retinitis pigmentosa, which is expected to begin in 2018.

Other Preclinical Product Candidates

In addition to our lead programs, we are developing a gene therapy product candidate for the treatment of cardiomyopathy associated with FA, a debilitating neurodegenerative disease resulting in poor coordination of legs and arms, progressive loss of the ability to walk, generalized weakness, loss of sensation, scoliosis, diabetes and cardiomyopathy as well as impaired vision, hearing and speech. It affects approximately 5,000 people in the U.S. and approximately 5,000 to 10,000 people in Europe. Currently, we are conducting observational studies and are in the early stages of preclinical development.

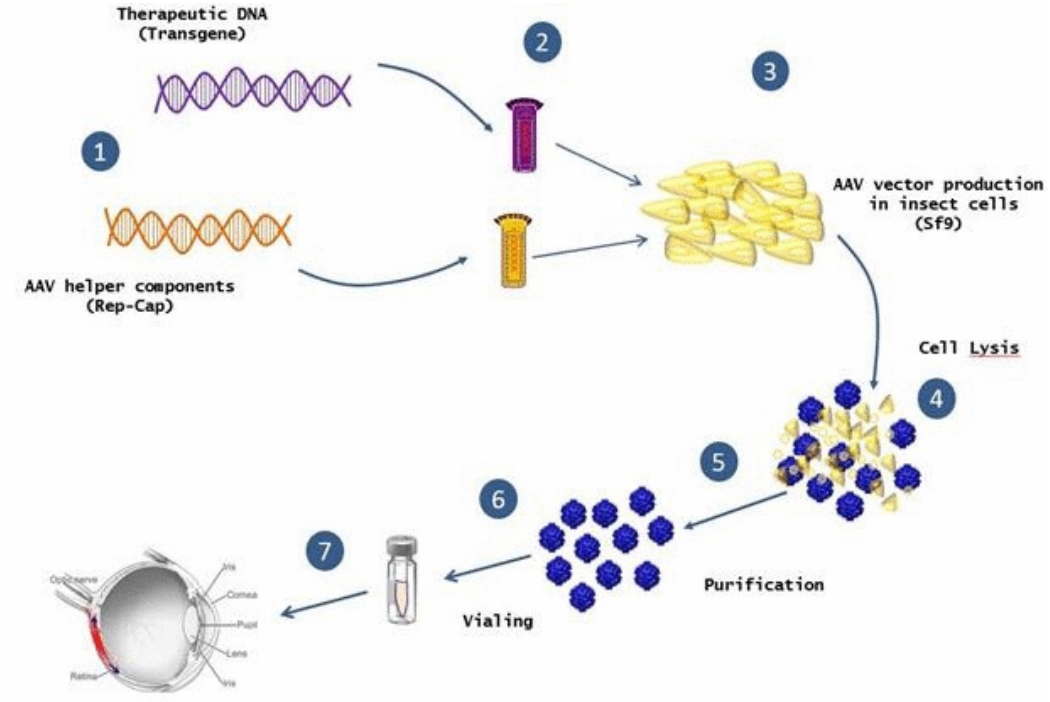
Manufacturing

Our AAV vector manufacturing process is based on the Baculovirus Expression Vector System ("BEVS"), which has been used in a number of FDA- and EMA-approved products. This approach is well suited for the production of large quantities of AAVs, as it takes advantage of the efficiency of viral infection coupled with the high density and scalability of insect cells grown in serum-free suspension cultures. Compared to the mammalian cell-based approaches commonly used in the field, our manufacturing process is designed to produce higher yields of vectors per manufacturing campaign in a cost-effective manner.

Our BEVS manufacturing process, using the eye as an example, is presented in the figure below.

1) The process begins with two DNA constructs, one encoding the therapeutic protein and the other encoding AAV helper components for the AAV capsid and replication of vectors.
2) Each DNA construct is inserted into the genome of a baculovirus to create two types of recombinant baculoviruses.
3) The two baculoviruses are used to transduce Sf9 insect cells, which in turn produce large amounts of AAV vectors containing the therapeutic gene of interest.
4) The transduced Sf9 insect cells are then harvested and treated with a lysis buffer solution to burst the insect cells and release the AAV vectors.
5) Recovered AAV vectors are then purified to remove unwanted debris.
6) Following purification, the vectors are formulated in a physiological solution and placed in vials.
7) The resulting drug product is ready for use as a therapeutic treatment for the targeted disease (e.g., injection in the eye to treat wAMD).

BEVS Manufacturing Process



Our AAV manufacturing method is industrialized, highly scalable and ready for adaptation for commercial stage. We believe our process provides the following advantages over competing systems:

- **Industrial-scale biologics production.** Our BEVS system can produce quantities of product required at commercial stage by incorporating scalable, well-established process steps used throughout the industry for biologic products.
- **Safety advantages.** Our BEVS system does not use mammalian cell cultures or tumorigenic cell lines, and the DNA sequences used to allow AAV vector production are inactive in mammalian cells, which lowers the risk of off-target expression from our products.
- **High yield and low cost.** Because of its scalability, our BEVS system allows the production of large quantities of AAV vectors up to one hundred times greater per manufacturing campaign than those obtained using conventional AAV production systems. This lowers the unit cost of goods and may enable us to meet global demand for large markets, such as wAMD.
- **High purity.** Our BEVS system coupled with our proprietary downstream purification process produces a highly pure drug substance.
- **Precedent regulatory framework.** Several FDA- and EMA-approved vaccines and gene therapy products including FluBlok, Cervarix and Glybera are manufactured using similar BEVS technology.

Our products are manufactured using proprietary cell banks and a scalable process developed internally that is transferred to approved Contract Manufacturing Organizations ("CMOs"). These CMOs produce investigational drugs under cGMP conditions to support our clinical trials. Raw materials of highest quality are purchased from various suppliers and are used throughout the manufacturing process.

We have entered into a manufacturing technology license agreement pursuant to which we and Lonza Houston, Inc. are assessing certain technology potentially useful for the manufacture of our products. The license agreement provides that the parties will conduct activities to evaluate such technology and that we may elect to engage Lonza to manufacture our products. We also granted to Lonza certain licenses to practice the manufacturing technology for products other than those being developed by us, our affiliates or sublicensees.

We continue to evaluate new raw material suppliers as well as CMOs with available manufacturing slots in order to provide manufacturing flexibility. As we prepare for larger, late-stage clinical trials and potential commercialization, we plan to begin the initial stage of investing in a manufacturing facility to build on our internal process development capabilities.

Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our AAV-based directed evolution platform, single-administration gene therapy candidates, and expertise in the field of gene therapy provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical, and biotechnology companies, as well as from academic institutions, governmental agencies, and public and private research institutions.

Our wAMD gene therapy ADVM-022 utilizes a proprietary vector and is administered through an intravitreal injection and will compete with a variety of therapies currently marketed and in development, including biologics, small molecules and gene therapy. Existing anti-VEGF therapies, Lucentis, EYLEA and Avastin, are well-established therapies and are widely accepted by physicians, patients and third-party payers as the standard-of-care treatment of patients with wAMD. To date, we are not aware of any treatment that has demonstrated a better benefit to patients than regular anti-VEGF protein delivery.

We know of a significant number of product candidates in development for wAMD, and we group them into four main categories:

- biosimilar anti-VEGFs
- combination / add-on therapy for efficacy improvement (for example, Anti-angiopoietin-2)
- next generation anti-VEGF with quarterly injection
- long acting delivery device / gene therapy to lower treatment frequency

There are several other companies with marketed products or products in development for the treatment of wAMD. These companies include Alcon, Allergan, Allegro Ophthalmics, LLC, Apellis Pharmaceuticals, Applied Genetic Technologies Corporation, Bayer, Hoffmann-La Roche Ltd., Iconic Therapeutics, Inc., Novartis, Ocular Therapeutix, Inc., Ohr Pharmaceuticals, Inc., Ophthotech Corporation, Opthea Limited, PanOptica Pharma, Quark Pharmaceuticals, SciFluor Life Science, LLC, Regeneron and REGENXBIO.

For the treatment of A1AT deficiency and HAE, we know of a number of products currently in development that aim to reduce the frequency of administration, improve the route of administration, and deliver better efficacy compared to the standard-of-care treatments available today. There are several companies with marketed products or products in clinical development for A1AT deficient patients with emphysema including Kamada Ltd., Shire and Grifols Therapeutics. For the treatment of HAE, there are several companies with marketed products or products in clinical development, including CSL Behring, Biocryst Pharmaceuticals, Ionis Pharmaceuticals, and Shire.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and commercializing those treatments. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. Our competitors' treatments may be more effective, or more effectively marketed and sold, than any treatment we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our treatments.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and subject registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payers.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, we expect that our therapeutic products, if approved, will be priced at a significant premium over competitive generic products and our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products.

Research and Development Expense

Our research and development expenses were $39.8 million, $31.7 million and $25.5 million for the years ended December 31, 2017, 2016 and 2015, respectively.

License and Collaboration Agreements

Regeneron

In May 2014, we entered into a collaboration agreement with Regeneron for an initial period of three years to research, develop and commercialize novel gene therapy products for the treatment of ophthalmologic diseases. These products are based on our proprietary viral vectors that express transgenes encoding molecules that modulate up to a total of eight specified targets, and encoding certain endogenous molecules known to bind to and modulate such targets (such products, including AVA-311, collectively the "Products"). In February 2017, Regeneron exercised its option to extend the research term of the collaboration agreement for an additional three years, through May 1, 2020.

Pursuant to the collaboration agreement, we and Regeneron have been conducting a research program to identify potential Products for a specified time period. Regeneron bears all costs of performing research under the Collaboration Agreement. Regeneron has a right to substitute a certain number of such targets and may, subject to a payment to us, expand the collaboration beyond the four initially designated targets to include up to four additional targets not currently being researched or developed by Adverum, and endogenous molecules known to bind to and modulate such additional targets, in the research program.

Regeneron has an option, exercisable with respect to all Products containing transgenes expressing molecules that modulate one of the specified targets, to obtain an exclusive, worldwide license to research, develop and commercialize such Products for the treatment, prevention or diagnosis of human disease or other medical disorders. Regeneron may exercise this option prior to the expiration of the term of the research program, within a certain time period after the acceptance for filing with the FDA of the IND for such Products. Regeneron must pay us an option fee each time it exercises an option.

Regeneron has the right to submit an IND with the FDA for Products prior to exercising its option. If Regeneron exercises its option for specified Products, Regeneron will be primarily responsible for developing, obtaining and maintaining regulatory approval for, and commercializing such Products.

We have a right to co-fund costs of developing, manufacturing and commercializing Products containing transgenes encoding molecules capable of modulating a target with respect to which Regeneron has exercised its option, subject to certain exceptions. We may exercise this co-funding right up to two times. If we exercise such right, we may elect to bear up to 35% of all development costs incurred for such Products. For any co-funded Products, Regeneron's payment obligations extend until the Products are no longer sold in the applicable territory. For those Products for which we exercise this option, either party may opt out of sharing development costs for all Products containing transgenes encoding molecules capable of modulating a protein target, in which case the other party may continue to develop and commercialize such Products, subject to the payment of a royalty to the other party ranging from low-single digit to low double-digit royalties. While Regeneron will record all revenue from sales of the co-funded Products, Regeneron will share in the net profits and losses of sales of any Products for which we exercised our co-funding right, with each party receiving a share of profits and bearing its share of losses in accordance with the share of development costs borne by each party for such Product, provided that neither party exercises its opt-out right for such Products.

Under the Collaboration Agreement, Regeneron made an initial payment of $8.0 million dollars for collaboration research costs, a one-time option fee and a one-time license grant fee.

In addition to the initial payment, Regeneron may make the following payments to us:

- Reimbursement for additional collaboration research costs;
- Up to $80.0 million in development and regulatory milestones for product candidates directed toward each of the eight therapeutic candidates, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets subject to the Collaboration Agreement; and
- Tiered, low- to mid-single digit royalties on annual net sales, subject to certain adjustments.

For each Product, Regeneron's payment obligations extend until the last to occur of the following: (i) the discontinuation of development of the Product or (ii) once a Product is approved by the FDA, the later of (x) the duration of patent coverage for the Product or (y) ten years after first commercial sale of the Product in a particular territory.

The collaboration agreement will expire with respect to each collaboration target upon expiration of all payment obligations by Regeneron. The collaboration agreement may also be terminated (i) by Regeneron at will, either in its entirety or on a target by target basis, upon 30 days' prior written notice to us, (ii) by either party, upon written notice in connection with a material breach remaining uncured 60 days after initial written notice, (iii) by us, if Regeneron challenges the patent rights licensed by us under the collaboration agreement or (iv) by either party, for insolvency of the other party.

Under our research, collaboration and license agreement with Regeneron, we are required to have a mutually agreed-on research plan with Regeneron in order to invoice Regeneron for services performed. We do not currently have a research plan in place, and, consequently, we are not currently receiving any reimbursements from Regeneron.

Editas

In August 2016, we entered into a collaboration, option, and license agreement with Editas pursuant to which we and Editas collaborate on certain studies using AAV vectors in connection with Editas' genome editing technology and we grant to Editas an exclusive option to obtain certain exclusive rights to use our proprietary vectors in up to five ophthalmic indications. We received a $1.0 million non-refundable upfront payment, with $0.5 million of such payment to be credited against Editas' obligation to fund research and development costs during the year ended December 31, 2016. Under the terms of the agreement, both we and Editas are subject to exclusivity obligations. In January 2018, we and Editas extended the collaboration, option and license agreement. In consideration of extending the agreement, Editas made a one-time payment of $0.5 million to us in February 2018.

Under the terms of the agreement, as amended, Editas may exercise the option with respect to a designated initial indication until September 30, 2018. With respect to the four other indications, Editas may exercise the option until the fourth anniversary of the effective date, provided that the option will expire on the third anniversary of the effective date if Editas has not exercised the option with respect to the initial indication or any other indication by such date. Upon Editas' timely exercise of the option with respect to the designated initial indication, Editas will pay us a $1.3 million fee. For the first additional indication for which Editas timely exercises its option, Editas will pay us a $1.5 million fee. Upon each subsequent exercise of the option, Editas will pay us a $1.0 million fee per indication. If Editas elects to develop a product using certain of our proprietary vectors, we will be eligible to receive up to $15.5 million in development and commercialization milestone payments for such product, and tiered royalties between the mid-single digits and low teens on net sales of such product, subject to certain adjustments.

Unless earlier terminated, the agreement will be in effect until the later of the expiration of the option exercise period or the expiration of the royalty term of the last product. At any time after the option is first exercised, Editas may terminate the Agreement for convenience in its entirety or on an indication-by-indication or country-by-country basis, upon prior written notice to us. We may also terminate the agreement if Editas challenges our patents relating to its proprietary vectors and does not withdraw such challenge within a defined period of time. In addition, either party may terminate the agreement with written notice upon a bankruptcy of the other party or upon an uncured material breach by the other party.

University of California

In May 2010, we entered into a license agreement with the Regents of University of California ("Regents"), as amended in September 2013. Under the license agreement, the Regents have granted to us an exclusive, even as to the Regents, license, with the right to grant sublicenses, under the Regents' undivided interest in patent rights covering a method of using recombinant gene delivery vectors for treating or preventing diseases of the eye, to develop and commercialize products covered by such patent rights in all fields of use in the U.S. The licensed patent rights are jointly owned by the Regents and Chiron Corporation, which was acquired by Novartis AG ("Chiron"), but our license extends only to the Regents' interest in such patent rights.

Under the license agreement, we are obligated to make milestone payments totaling up to $0.9 million upon reaching certain stages of development of the licensed products for one indication and totaling up to $0.5 million for each subsequent indication for which licensed products are developed, for up to a maximum of two additional indications. Through December 31, 2017, none of these goals had been achieved, and no milestones were payable. The license agreement also contains certain royalty payment requirements for net sales of licensed products.

Our license agreement with the Regents continues in effect for the life of the last-to-expire patent. We expect the agreement to terminate prior to any commercialization of any product candidates to which they apply. We may terminate this agreement without cause at any time upon 30 days' prior written notice to the Regents. The Regents may terminate this agreement for a breach by us that remains uncured for 60 days, if we become insolvent, if we directly or through a third-party file a claim that a licensed patent right is invalid or unenforceable or if we fail to meet or extend the date for meeting certain diligence milestones.

Cornell University

We were a party to a master service agreement ("MSA") with Cornell University ("Cornell") originally established in August 2014 and amended in December 2015. Under the MSA, Cornell provided assistance in regulatory affairs, overall project management, and parameter development. The MSA, as amended, provided for Annapurna to pay Cornell $13.3 million ratably over 4 years for these services as services were performed.

In December 2016, we informed Cornell that we decided to terminate the MSA for material breach, effective January 6, 2017. Subsequently, Cornell informed us that it disputes the validity of our termination of the MSA. Although we intend to defend the validity of our termination of the MSA, we recorded $2.0 million of estimated costs associated with the termination of the MSA during the year ended December 31, 2017. This MSA included services relating to our gene therapy programs ADVM-043, ADVM-053 and severe allergy. Our three licensing agreements with Cornell for these programs remain unchanged.

The decision to terminate the MSA was due to Cornell's failure to deliver therapeutic material of ADVM-043 suitable for use in human patients. As a result of this decision, we contracted with a large-scale contract manufacturing organization that complies with cGMP industry standards and can produce product quantities for both our planned clinical trials and potential commercial supply. This was part of our planned upgrade of the manufacturing process for ADVM-043, implementing our proprietary, highly-scalable baculovirus-based production system, in advance of our initiation of the ADVANCE trial in the fourth quarter of 2017.

In December 2015, Annapurna entered into three licensing agreements with Cornell, pursuant to which we are advancing gene therapy programs ADVM-043, ADVM-053, and severe allergy, which originally were initiated at the Department of Genetic Medicine at Weill Cornell.

A1AT Deficiency License Agreement: Under this agreement, we hold an exclusive license to certain know-how related to A1AT deficiency and rights to an IND application to initiate clinical studies of gene therapy for A1AT.

HAE License Agreement: Under this agreement, we hold an exclusive license to certain technology related to HAE and a non-exclusive license to certain other intellectual property related to the HAE program.

Allergy License Agreement: Under this agreement, we hold an exclusive license to certain patents related to allergens and a non-exclusive license to certain other technology related to allergens.

Across these three license agreements, Cornell is entitled to receive aggregate annual maintenance fees ranging from $30,000 to $0.3 million per year, up to $16.0 million in aggregate milestone payments and royalties on sales in the low single-digits, subject to adjustments and minimum thresholds.

We may terminate any of these license agreements for convenience upon ninety days written notice. Cornell may terminate any of the license agreements for material breach if such breach is not cured within a specified number of days. Cornell may also terminate the HAE License Agreement and/or the Allergy License Agreement if we commence any action and file a written claim asserting that any portion of the licensed patent rights is invalid or unenforceable.

Dr. Crystal, Chairman of Genetic Medicine, the Bruce Webster Professor of Internal Medicine and a Professor of Genetic Medicine and of Medicine at Weill Cornell, served as a consultant to Annapurna since inception and continues to provide services to us for an annual base compensation of $0.2 million.

REGENXBIO

A1AT Deficiency/Allergy License Agreement: In October 2015, we entered into an exclusive worldwide license with REGENXBIO to certain intellectual property in order to develop and commercialize products for the treatment of A1AT deficiency. Under this agreement, we also had an option to be granted an exclusive worldwide license to certain intellectual property to develop and

commercialize products for the treatment of severe allergies, however this option was not exercised, and expired in October 2016. Under this license agreement, REGENXBIO was eligible to receive annual maintenance fees, up to approximately $20.0 million in combined milestone payments and royalties in the mid-to-high single digits. In April 2017, we notified REGENXBIO that we exercised our right to terminate this license agreement for any reason upon six months' written notice. The termination was effective in October 2017.

FA License Agreement: In April 2014, we entered into an exclusive worldwide license to certain intellectual property in order to develop and commercialize products using the AAVrh.10 vector for FA, where the vector is administered by any route except directly to the central nervous system ("FA Systemic").

Under the terms of this license agreement, we also had options to obtain a non-exclusive worldwide license to develop and commercialize an FA product where the vector is administered directly to the central nervous system ("FA CNS"), as well as an FA Systemic product using another AAV vector. The option to obtain a non-exclusive license to FA Systemic expired in April 2015 and the option to obtain a non-exclusive license for FA CNS expired in April 2016, and neither were exercised. In October 2017, we notified REGENXBIO that we exercised our right to terminate this license agreement for any reason upon six months' written notice. The termination will be effective in April 2018.

Inserm Transfert

In July 2014, we entered into an agreement with Inserm Transfert ("Inserm") whereby we hold an exclusive license to certain patents to develop and commercialize products for the treatment of FA and a non-exclusive license to certain other intellectual property related to the FA program. The agreement was amended in October 2015 to increase the scope of the intellectual property under the licenses. Under this agreement, Inserm is entitled to receive certain de minimis license payments, certain development milestone payments of up to approximately €2.0 million in the aggregate and royalties on sales in the low single-digits, subject to adjustments.

Unless earlier terminated, this agreement will be in effect on a country-by-country, licensed product-by-licensed product basis until the later of the expiration of the last claim of the licensed intellectual property which cover the manufacture, use or sale of such product in such country or 10 years after the first commercial sale of such product in such country in which such product is sold. Upon a country-by-country and product-by-product basis, Annapurna will have a fully paid up, perpetual, irrevocable license with respect to such product in such country under the licensed intellectual property following expiration of this agreement with respect to such product in the applicable country. Annapurna may terminate this agreement upon 60 days' prior written notice. Inserm may terminate this license agreement if Annapurna becomes the subject of a voluntary or involuntary petition in bankruptcy or fails to meet development milestones and such failure is not cured within a specified number of days. Inserm may also terminate the license granted to Annapurna in a given country if Annapurna (i) before regulatory approval of a product in any country, has ceased conducting any development of products in all countries for 12 consecutive months or (ii) after regulatory approval of a product in a given country, has ceased marketing such product in such country for 12 consecutive months.

Pursuant to Section 4.7 of the agreement with Inserm, our acquisition of Annapurna triggered a one-time payment to Inserm of €0.3 million.

Intellectual Property

Overview

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy that may be important for the development of our business. We additionally may rely on regulatory protection afforded through orphan drug designations, data exclusivity, market exclusivity, and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; obtain regulatory exclusivity and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. In some cases, these rights may need to be enforced by third party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

We own or license more than 60 patent applications pending in the U.S. and foreign jurisdictions. More than 50 patent applications have been filed in the U.S. and foreign jurisdictions by or on behalf of universities which have granted us exclusive license rights to the technology. To date, more than 20 patents have been issued to us or to our licensors that are active. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek patent protection in the U.S. and abroad for a variety of technologies, including: research tools and methods, AAV-based biological products, methods for treating diseases of interest and methods for manufacturing our AAV-based products. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel biological products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use specific technologies in our research and development.

Company-owned Intellectual Property

We own three families of patent applications that are directed to AAV-based compositions and methods for treating or preventing eye diseases associated with neovascularization. Applications in the first of these families relate to an AAV gene therapy for the treatment of wAMD using an anti-VEGF composition, various unit dosages, dosing regimens and routes of administration. Applications in this family are pending in the U.S., and corresponding patent applications are pending elsewhere in North America, Europe, and Asia. Patents that may eventually issue from this patent family, if any, are generally expected to expire in 2033, subject to possible patent term extensions. Applications in the second and third of these families relate to AAV gene therapy for the treatment of wAMD using the 7m8 vector to deliver ranibizumab or aflibercept. Each family has an application pending in the U.S. and a corresponding pending PCT application. Patents that may eventually issue from either of these patent families, if any, are generally expected to expire in 2037, subject to possible patent term extensions.

We also own seven families of patent applications that are directed to various aspects of our proprietary technology platform. These families contain pending U.S. provisional or PCT applications or national phase applications in the U.S., elsewhere in North America, Europe, and Asia. Patents that may eventually issue from these families, if any, are generally expected to expire between 2036 and 2038, subject to possible patent term extensions.

We are also pursuing innovative ways to regulate the expression of transgenes in tissues. To that end, we have, in collaboration with Stanford University, filed a U.S. patent application that is directed to methods for regulating gene expression in a subject. Patents that grant from this application, if any, are expected to expire in 2033, subject to possible patent term extensions.

Licensed Intellectual Property

We have obtained both exclusive and non-exclusive licenses to patents directed to both compositions of matter and methods of use and to other intellectual property.

For example, we have exclusively licensed several families of patents and patent applications that relate to variant rAAV virions having desirable characteristics, such as increased infectivity, as well as novel methods to screen for such variants.

One patent family that we have exclusively licensed includes granted patents in the U.S., as well as elsewhere in North America and Europe, as well as a pending patent application in Canada. The patents in this family are projected to expire in 2024, subject to possible patent term extensions.

Another patent family that we have exclusively licensed includes granted U.S. patents that are projected to expire in 2031 and a pending U.S. patent application that, if granted, is also projected to expire in 2031, in both cases subject to possible patent term extensions.

A third patent family that we have exclusively licensed includes claims directed to the novel AAV7m8 vector, which allows delivery of transgenes to the retina via intravitreal injection, and which we utilize in clinical candidates ADVM-022 and ADVM-032. This family includes issued patents in the U.S., as well as elsewhere in North America, Europe, Asia, and the Pacific. Corresponding applications are pending in the U.S. and elsewhere in North America, Asia and the Pacific. Patents that issue from this patent family, if any, are generally expected to expire in 2032, subject to possible patent term extensions.

We have also nonexclusively licensed rights to a patent family that includes issued patents in the U.S., Europe, and Asia. These patents are expected to expire in 2027, subject to possible patent term extensions.

We have exclusively licensed a family of patent applications related to gene therapy treatments for HAE, C1-esterase deficiency, which includes pending U.S. and foreign applications. Patents that grant from this patent family, if any, are generally expected to expire in 2036, subject to possible patent term extensions and adjustments.

We have exclusively licensed a family of patent applications related to gene therapy treatments for severe allergies, which includes pending U.S. and foreign applications. Patents that grant from this patent family, if any, are generally expected to expire in 2036, subject to patent term extensions and adjustments.

We have exclusively licensed a family of patents and applications related to the treatment of cardiomyopathy associated with FA. This family includes a granted US patent and pending applications in the U.S. and elsewhere in North America, Europe, Asia, and the Pacific. Patents that grant from this patent family, if any, are generally expected to expire in 2033, subject to possible patent term extensions and adjustments.

We have also exclusively licensed a patent family directed to the use of certain rAAVs for use in FA Systemic including pending applications in Australia, Canada, China, Europe, Hungary, Israel, Japan, New Zealand and the U.S. patents that grant from this patent family, if any, are generally expected to expire in 2022, subject to possible patent term extensions and adjustments.

We have exclusively licensed certain know-how related to gene therapy for A1AT deficiency and rights to an IND to initiate clinical studies of gene therapy for A1AT.

Trade Secret Protection

Finally, we may rely, in some circumstances, on trade secrets to protect our technology, including with regard to technology or other aspects of our product candidates for which we do not obtain patent protection. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacturing, marketing and distribution of drug product and biologic product candidates. These agencies and other federal, state and local entities regulate the research, development, testing, manufacturing, quality control, approval, labeling, storage, record keeping, advertising, promotion, distribution, post-approval monitoring and reporting, sampling, and export and import of our product candidates.

In the U.S., the FDA regulates drug and biologic products under the Federal Food, Drug, and Cosmetic Act ("FFDCA"), and the FDA implements regulations and other laws, including, in the case of biologics, the Public Health Service Act. 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 post-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, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on our business, financial condition, results of operations and prospects. Biologics require the submission of a Biologics License Application ("BLA") and approval by the FDA before being marketed in the U.S. Similarly, FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the U.S.

Within the FDA, the Center for Biologics Evaluation and Research ("CBER") regulates gene therapy products. Within CBER, the review of gene therapy and related products is consolidated in the Office of Tissues and Advanced Therapies and FDA has established the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER in its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health ("NIH") are also subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee ("RAC"), which will soon only publicly review clinical trials if the trials cannot be evaluated by standard oversight bodies and pose unusual risks. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC public review process can delay the initiation of a clinical trial. Similarly, the FDA can put an IND on clinical hold even if the RAC provides an exemption from an in-depth, public review. The FDA and the NIH have published guidance documents with respect to the development and submission of gene therapy protocols. The FDA also has published guidance documents related to, among other things, gene therapy products IND applications; FDA guidance documents provide the current thinking about a particular subject, yet are not legally binding. However, products in this area are novel and present highly complex scientific and medical issues, making the predictability of FDA's policies and practices in this area less certain.

The process required by the FDA before our product candidates may be marketed in the U.S. generally involves:

- Completion of non-clinical laboratory tests, preclinical studies and formulation studies all performed in accordance with current Good Laboratory Practice ("GLP") regulations;
- Submission of an IND to the FDA, which must become effective before human clinical trials may begin;
- Approval by an independent institutional review board ("IRB"), at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials according to Good Clinical Practice ("GCP"), and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the drug candidate for its proposed indication;
- Performance of clinical trial product manufactured under cGMP to establish the identity, strength, quality, purity or potency of the product;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug or biologic is produced, prior to commercialization, to assess compliance with cGMP, regulations, and any additional requirements pertaining to the manufacture and distribution of drug and biologic products;
- Submission to the FDA of a BLA for marketing approval that includes substantial evidence of purity and potency, safety and efficacy from results of nonclinical testing and clinical trials;
- Successful completion of FDA audit(s) of the nonclinical and clinical trial sites that generated the data in support of the BLA;
- Successful completion of the advisory committee review, if FDA convenes an advisory committee; and
- Payment of user fees and FDA review and approval, or licensure, of the BLA prior to any commercial marketing, sale or shipment of the product.

The preclinical 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.

Before testing any drug product or biologic product candidate, including a gene therapy product, in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs.

Our gene therapy studies involve recombinant DNA research, and therefore compliance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules ("NIH Guidelines") is mandatory. Appropriate protocol(s) and related documentations are submitted to, and the study is registered with, the NIH Office of Biotechnology Activities ("OBA"), pursuant to the NIH Guidelines. The NIH is responsible for convening the Recombinant DNA Advisory Committee ("RAC") that will discuss the protocol(s) including issues that raise novel or particularly important scientific, safety or ethical considerations. The OBA will notify the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. RAC proceedings and reports are posted to the OBA website and can be accessed by the public.

The results of preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical trial protocol, are submitted as part of an IND to the FDA. Some preclinical testing may continue even after the IND is submitted. The OBA notifies the FDA of the RAC's decision regarding the necessity for full public review of a gene therapy protocol. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to the content(s) of the IND that could potentially expose human research subjects to health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the IND goes into effect and the clinical trial can begin. With gene therapy protocols, if the FDA allows the IND to proceed, but the RAC decides that full public review of the protocol is warranted, the FDA will request at the completion of its IND review that sponsors delay initiation of the protocol until after completion of the RAC review process. The FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold on an IND, clinical trials may not commence or recommence without FDA authorization and then only under terms authorized by FDA.

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of qualified investigators, generally physicians not employed by or under the study sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, the parameters to be used in monitoring subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur, and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND. An IRB for each medical center proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. Clinical testing also must satisfy GCP requirements, including the requirements for informed consent from all subjects. FDA usually recommends that sponsors observe all surviving subjects who receive treatment using gene therapies in clinical trials for potential gene therapy-related delayed adverse events for a minimum 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire. FDA does not require the long-term tracking to be complete prior to its review of the BLA.

All clinical research performed in the United States in support of a BLA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, under FDA regulations at 21 CFR 312.120, FDA will accept a well-designed, well-conducted, non-IND foreign study as support for an application for marketing approval if (i) the study was conducted in accordance with GCP as further detailed in the regulation, including review and approval by an independent ethics committee, and (ii) if FDA is able to validate the data from the study through an onsite inspection, if necessary. In addition, FDA requires that a sponsor or applicant who submits data from a foreign clinical study not conducted under an IND as support for a marketing application submit, in addition to other required information, a description of the actions the sponsor or applicant took to ensure that the research conformed to GCP. Further, when a sponsor intends for marketing approval of a new drug to be based solely on foreign clinical data, additional requirements apply that are described in FDA regulations.

Clinical Trials

For purposes of BLA submission and approval, clinical trials are typically conducted in three or four sequential phases, which may overlap or be combined.

- Phase 1: Clinical trials are initially conducted in a limited population of subjects to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.
- Phase 2: Clinical trials are typically well-controlled, closely monitored studies that are generally conducted in a limited subject population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the product candidate for specific targeted indications in subjects with the disease or condition under study.

- Phase 3: Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as "pivotal" studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. Phase 3 clinical trials are generally undertaken with large numbers of subjects, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse subject population at multiple, geographically-dispersed clinical trial sites.
- Phase 4: In some cases, the FDA may condition approval of a BLA for a product candidate on the sponsor's agreement to conduct additional clinical trials after the product's approval. In other cases, a sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the product. Such post approval trials are typically referred to as Phase 4 clinical trials or post-marketing or post approval studies.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider at each of the above stages of development and relate to, among other things: the proper preclinical assessment of gene therapies; the chemistry, manufacturing and control information that should be included in an IND application; the proper design of tests to measure product potency in support of an IND or BLA application; and measures to observe delayed adverse effects in subjects who have been exposed to investigational gene therapies when the risk of such effects is high. Further, the FDA usually recommends that sponsors observe subjects for potential gene therapy-related delayed adverse events for a 15-year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire. The NIH and the FDA have a publicly accessible database, the Genetic Modification Clinical Research Information System, which includes information on gene therapy trials and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these trials.

Per the regulations, a sponsor (in industry or academia) of a clinical trial must register a clinical trial on the ClinicalTrials.gov website, the registry of new and on-going clinical trials of drugs, biologics, and device products. Sponsors are required to maintain the currency of the posting of the clinical trials posted on-line in the registry. This clinical trial registry and results data bank for clinical trials also contains summary results information on a clinical trial including adverse event information from the clinical trials and for pediatric post-market surveillance of a device product. The registry also provides information that helps patients find trials for which they might be eligible, enhance the design of clinical trials and prevent duplication of unsuccessful or unsafe trials, improve the evidence base that informs clinical care, increase the efficiency of drug and device development processes, improve clinical research practice, and build public trust in clinical research. These phases of testing may not be completed successfully within any specified period, if at all. Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the product candidate in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Biologics License Applications

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the product, are submitted to the FDA in the form of a BLA requesting approval to market the product for one or more specified indications. The submission of a BLA must be accompanied by a substantial user fee unless a waiver applies, and is subject to a sixty day filing review period to determine if the application is substantially complete to permit substantive review. Given our current company size and likely growth over the next years prior to a BLA submission, we would likely submit for a waiver to the Prescription Drug User Fee Act ("PDUFA") fees based on our company size and it being our first BLA.

Under the PDUFA, the FDA has a performance goal to review applications within 6 months for priority reviews or 10 months for standard reviews. The review timeline begins upon FDA's acceptance of the original application submission for filing, no later than 60 calendar days from the date FDA receives the application. In some instances, the review process and the PDUFA goal date may be extended depending on the information required in order the FDA reviewers to complete their review of the BLA.

The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of a BLA if the applicable statutory and regulatory criteria are not satisfied, which may require additional clinical data or an additional Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. Moreover, even if a product receives approval, the approval may be significantly limited to specific disease and dosages or the indications for use may otherwise be limited or subject to Risk Evaluation and Mitigation Strategies, which could restrict the commercial value of the product. Once the FDA approves a BLA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. Where a withdrawal may not be appropriate, the FDA still may seize existing inventory of such product or require a recall of any biologic or drug already on the market. In addition, the FDA may require testing, including Phase 4 clinical trials and surveillance programs to monitor the effect of approved biologics which have been commercialized. The FDA has the authority to prevent or limit further marketing of a biologic or drug based on the results of these post-marketing programs.

Biologics may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the product, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Before approving a BLA, the FDA will inspect the facility or the facilities at which the finished biologic or drug product, and sometimes, for drug products, the active drug ingredient, is manufactured, and will not approve the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance and will not approve the product unless compliance with IND study requirements and GCP requirements is satisfactory.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our product candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Preclinical and clinical data may be interpreted by the FDA in different ways, which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the biologic. After approval, certain changes to the approved product, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval. Depending on the nature of the change proposed, a BLA supplement must be filed and approved before the change may be implemented. For many proposed post-approval changes to a BLA, the FDA has up to 180 days to review the application. As with new BLAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

In addition, prior to submitting a BLA for a new biologic, a sponsor may be able to take advantage of one or more FDA programs that are intended to facilitate and expedite development and review of new drugs to address unmet medical need in the treatment of a serious or life-threatening condition (e.g., priority review, fast track designation) provided the product meets the criteria for those programs. While some of these programs have been in existence for a number of years, Congress established additional programs intended to expedite the development of drugs and biologics in the recently enacted 21st Century Cures Act (Cures Act), which was signed into law on December 13, 2016. Notably with respect to gene therapy products, section 3012 of the Cures Act clarifies the authority of FDA to facilitate the development, review, and approval of "genetically targeted drugs" and "variant protein targeted drugs" to address an unmet medical need in one or more patient subgroups, including subgroups of patients with different mutations of a gene, with respect to rare diseases or conditions that are serious or life-threatening. 21st Century Cures Act Section 3033 also

established a regenerative advanced therapy designation process intended to expedite the development of regenerative medicine therapies, defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations, that are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition.

Other Regulatory Requirements

Any biologics manufactured or distributed by us or our collaborators pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the product. Biologic and drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon us and our third party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a product from distribution or withdraw approval of the BLA for that biologic.

The FDA closely regulates the post-approval marketing and promotion of biologics and drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Under FDA's current interpretation of the relevant laws, in proactively promoting a drug, a company generally can make only those substantiated claims relating to safety and efficacy that are for indications approved by the FDA and that are otherwise consistent with the FDA-approved label for the drug or biologic. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

Other Healthcare Laws and Regulations

If we obtain regulatory approval for any of our product candidates, we may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. 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, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- Federal false claims laws, including the False Claims Act and civil monetary penalty law, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;
- Federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- The federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services ("CMS") information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- Health Insurance Portability and Accountability Act, as amended by Health Information Technology for Economic and Clinical Health Act, which governs and protects the security and privacy of individually identifiable health information of certain health plans, healthcare clearinghouses and healthcare providers, and their respective business associates that perform services for them involving individually identifiable health information; and
- State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; 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.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs, imprisonment, and additional reporting requirements and oversight if become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, recent events in the pharmaceutical and biotechnology industry generally have resulted in increased public and governmental scrutiny of the cost of drugs. In particular, U.S. federal prosecutors have issued subpoenas to pharmaceutical companies seeking information about drug pricing practices and the U.S. Senate is investigating several pharmaceutical companies relating to drug price increases and pricing practices. If we obtain regulatory approval of any of our product candidates, our revenue and future profitability could be negatively affected if these inquiries were to result in legislative or regulatory proposals that limit our ability to increase the prices of our products.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the U.S. 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 payers. Third-party payers include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payer will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a payer'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. A number of gene therapy products have been approved over the past year by the FDA. Although the CMS subsequently approved its first method of coverage and reimbursement for one such product, the methodology has been subject to challenge by members of Congress. CMS's decision as to coverage and reimbursement for one product does not mean that all similar products will be eligible for analogous coverage and reimbursement. As there is no uniform policy for coverage and reimbursement amongst third-party payors in the United States, even if CMS approves coverage and reimbursement for any of our product candidates, it is unclear what affect, if any, such a decision will have on our ability to obtain and maintain coverage and adequate reimbursement from other private payors.

Third-party payers 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 payers 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 United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, contains provisions that may reduce the profitability of drug products, including, for example, increased the minimum rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care plans, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are

inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals. In addition, following the November 2016 Presidential election in the United States, significant uncertainty exists regarding the future of the Affordable Care Act. It is possible that there will be legislation in the future either to amend or replace the Affordable Care Act and that such new legislation will be generally unfavorable toward the pharmaceutical and biotechnology industries (including with regard to a possible reduction in the number of insured individuals with access to drug coverage or additional measures aimed at high cost drug and biologic products). At this time, it is unclear whether those changes will also have an impact on biologic product exclusivity or the biosimilar product licensure pathway established under the Biologics Price Competition and Innovation Act (BPCIA), which was enacted as part of the Affordable Care Act.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payers fail to provide adequate coverage and reimbursement. In addition, emphasis on cost containment measures in the U.S. 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.

International Regulation

In addition to regulations in the U.S., we or our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our future drugs. Whether or not we obtain FDA approval for a drug, we or our collaborators must obtain approval of a drug by the comparable regulatory authorities of foreign countries before commencing clinical trials or marketing of the drug in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized, decentralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marking authorization that is valid for all European Union member states. The decentralized procedure includes selecting one reference member state (RMS), and submitting to more than one EU member state at the same time. The RMS National Competent Authority conducts a detailed review and prepares an assessment report, to which concerned member states provide comment. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marking authorization may submit an application to the remaining member states post-initial approval. Under the centralized procedure, within 120 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we or our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of our future drugs.

Environmental Regulation

We are subject to numerous foreign, federal, state and local environmental, health and safety laws and regulations relating to, among other matters, safe working conditions, product stewardship and end-of-life handling or disposition of products, and environmental protection, including those governing the generation, storage, handling, use, transportation and disposal of hazardous or potentially hazardous materials. Some of these laws and regulations require us to obtain licenses or permits to conduct our operations. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, including requirements in the European Union relating to the restriction of use of hazardous substances in products, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits.

Segment and Geographic Information

We operate and manage our business as one reporting and operating segment, which is the business of developing and commercializing gene therapeutics. Our chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance.

To date, we have not generated any revenue from product sales and our revenues are generated in the U.S. Substantially all of our non-monetary long-lived assets are located in the U.S.

Employees

As of February 28, 2018, we had 78 full-time employees, including a total of 17 employees with M.D., DVM or Ph.D. degrees. Within our workforce, 56 employees are engaged in research and development and 22 in business development, finance, legal, human resources, facilities, information technology and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements.

Corporate and Available Information

We were incorporated in Delaware in 2006 under the name "Avalanche Biotechnologies, Inc." We completed the initial public offering of our common stock in August 2014. On May 11, 2016, upon the completion of our acquisition of Annapurna Therapeutics SAS, we changed our name to "Adverum Biotechnologies, Inc." Our common stock is currently listed on The Nasdaq Global Market under the symbol "ADVM" We are an "emerging growth company" under the Jumpstart Our Business Startups Act of 2012, and therefore we are subject to reduced public company reporting requirements.

Our principal executive offices are located at 1035 O'Brien Drive, Menlo Park, CA 94025, and our telephone number is (650) 272-6269. Our website address is www.adverum.com. We make available on our website, free of charge, our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. Further, a copy of this Annual Report on Form 10-K is located at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D. C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov. The information found on our website is not incorporated by reference into this Annual Report on Form 10-K or any other report we file with or furnish to the SEC.

Item 1A. Risk Factors

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. The risks described below are not the only risks facing the Company. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, results of operations and prospects.

Risks Related to Our Financial Position and Need for Capital

We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since we were founded in 2006 and expect to incur significant losses for the foreseeable future as we continue development of our product candidates. As of December 31, 2017, we had an accumulated deficit of $254.1 million. Losses have resulted principally from costs incurred in our clinical trials for our prior wAMD product candidate, AVA-101, research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities and, if any of our product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize any of our product candidates. We do not currently have the required approvals to market any of our product candidates, and we may never receive such approvals. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

We expect that our cash and cash equivalents will be sufficient to fund our lead gene therapy programs through the end of 2019. If this expectation proves to be wrong, we may be forced to delay, limit or terminate certain of our development efforts.

As of December 31, 2017, our cash, cash equivalents and short-term investments were approximately $190.5 million. We currently expect this cash, cash equivalents and short-term investments, together with the net proceeds from our February 2018 underwritten public offering of our common stock, to fund our planned operations through the end of 2019. However, this estimate is based on a number of assumptions that may prove to be wrong, including our expectations about the timing of planned clinical trials, and changing circumstances beyond our control may cause capital to be consumed more rapidly than currently anticipated. As a result, our operating plan may change, and we may need to seek additional funds sooner than planned, through collaboration agreements and public or private financings. If we run low on capital before we are able to achieve meaningful clinical data for some or all of our lead product candidates, we may be unable to successfully raise additional funds, and, consequentially, may need to significantly curtail some or all of our development activities.

We will need to raise additional funding, which may not be available on acceptable terms, or at all. If we fail to obtain additional capital necessary to fund our operations, we will be unable to successfully develop and commercialize our product candidates.

We will require substantial future capital in order to complete the preclinical and clinical development for our product candidates and to potentially commercialize these product candidates. Any future clinical trials of our product candidates would cause an increase in our spending levels, as would other corporate activities. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the type, number, scope, progress, expansion costs, results of and timing of any future preclinical studies and clinical trials of any of our product candidates which we are pursuing or may choose to pursue in the future;
- the need for, and the progress, costs and results of, any additional clinical trials or nonclinical studies of our product candidates we may initiate based on the results of any clinical trials that we may plan or discussions with the FDA, including any additional clinical trials or nonclinical studies the FDA or other regulatory agencies may require evaluating the safety of our product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining or maintaining manufacturing for our product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales and marketing capabilities and enhanced internal controls over financial reporting;
- the terms and timing of establishing collaborations, license agreements and other partnerships;
- costs associated with any new product candidates that we may develop, in-license or acquire;

- the effect of competing technological and market developments;
- our ability to establish and maintain partnering arrangements for development; and
- the costs associated with being a public company.

Some of these factors are outside of our control. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of our clinical trials and remaining development program through commercial introduction. We expect that we will need to raise additional funds in the future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through collaboration agreements and public or private financings. Additional funding may not be available to us on acceptable terms or at all and the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we will be unable to complete any future clinical trials for our product candidates and we may be required to significantly curtail some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or some of our technologies or otherwise agree to terms unfavorable to us.

Risks Related to the Discovery and Development of Our Product Candidates

Our business will depend substantially on the success of one or more of ADVM-043, ADVM-053, and ADVM-022, our lead product candidates. If we are unable to develop, obtain regulatory approval for, or successfully commercialize, any or all of our lead product candidates, our business will be materially harmed.

Our lead product candidates are in the early stages of development and will require substantial clinical development and testing, manufacturing bridging studies, process validation and regulatory approval prior to commercialization. We are conducting the ADVANCE trial in patients with A1AT deficiency and we are continuing pre-clinical development of our other lead product candidates to support planned INDs in the second half of 2018. It is critical to our business to successfully develop and ultimately obtain regulatory approval for one or more of these lead product candidates. Our ability to commercialize our product candidates effectively will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our lead product candidates;
- receipt of marketing approvals for any future products for which we complete clinical trials, including securing regulatory exclusivity to the extent available;
- establishing commercial manufacturing capabilities, for example, by making arrangements with third-party manufacturers that can provide adequate and quality products and services to support clinical development and the market demand for our product candidates, if approved;
- successfully launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product as a viable treatment option by patients, the medical community and third-party payers;
- establishing market share while competing with other therapies;
- a continued acceptable safety profile of our products following regulatory approval;
- maintaining compliance with post-approval regulation and other requirements; and
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates.

If we, or our collaborators, do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to commercialize our product candidates, which would materially and adversely affect our business, financial condition, results of operations and prospects.

Moreover, of the large number of biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a biologics license application ("BLA") to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market any of our lead product candidates, any such approval may be subject to limitations on the indicated uses for which we may market the product, or limitations related to its distribution. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, there can be no assurance that any of our product candidates will be successfully developed or commercialized. If we decide to invest in the continued development and potential commercialization of any or all of our lead product candidates and we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, such product candidates, we may not be able to generate sufficient revenue to continue our business.

Our gene therapy platform is based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We have concentrated our research and development efforts on our gene therapy platform and our future success depends on the successful development of product candidates based on this platform. There can be no assurance that any development problems we experience in the future related to our platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical trials or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical trial requirements of the FDA, the European Medicines Agency ("EMA") and other regulatory agencies and the criteria these regulators may use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. The FDA recently approved its first vector-based human gene therapy product, LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

Regulatory requirements governing gene and cell therapy products may change in the future. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the National Institutes of Health ("NIH") may also be subject to review by the NIH Office of Science Policy's Recombinant DNA Advisory Committee ("RAC"). Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the study and approved its initiation. Clinical trial sites in the U.S. that receive NIH funding for research involving recombinant or synthetic nucleic acid molecules are required to follow RAC recommendations, or risk losing NIH funding for such research or needing NIH pre-approval before conducting such research.

Conversely, the FDA can put an IND on clinical hold even if the RAC has provided a favorable review of the gene transfer protocol. Also, before a clinical study can begin at an NIH-funded institution, that entity's institutional review board ("IRB") and its Institutional Biosafety Committee will have to review the proposed clinical trial to assess the safety of the study. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for human research on or approval of any of our product candidates.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we may be required to consult with these regulatory and advisory groups, and comply with applicable guidelines or recommendations. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

We may not be successful in our efforts to identify or discover additional product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our platform. Our research programs, including those subject to our collaborations with Regeneron and Editas, may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business, financial condition, results of operations, and prospects and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

Except for our recently-initiated ADVANCE Phase 1/2 trial, we have not tested any of our internally-developed viral vectors or product candidates in clinical trials.

Drug development has inherent risk. Except for our ADVANCE Phase 1/2 trial, which was initiated in December 2017, none of our current product candidates has been evaluated in human clinical trials, and we may experience unexpected results in the future. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates containing our proprietary vectors are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials may not have favorable results in later clinical trials, if any, or receive regulatory approval.

If our proprietary vectors are not shown to be safe and effective, we may not realize the value of our investment in our technology. In addition, success in pre-clinical studies or in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through pre-clinical and initial clinical testing. Furthermore, any future trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of products under development result in the submission of a BLA to the FDA and even fewer are approved for commercialization.

We cannot confirm that results from any clinical trials that we plan will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

Preliminary and interim data from our clinical trials that we may announce or publish from time to time may change as more patient data become available.

From time to time, we may announce or publish preliminary or interim data from our clinical trials. Preliminary and interim results of a clinical trial are not necessarily predictive of final results.

Preliminary and interim data are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues or further patient follow up occurs and more patient data become available. As a result, preliminary and interim data should be viewed with caution until the final data from a locked database are available. Material adverse changes in the final data compared to the interim data could significantly harm our business, prospects, financial condition and results of operations.

Our product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA and by comparable regulatory authorities in foreign markets. In the U.S., we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved, as well as the target indications and patient population. Approval policies or regulations may change, and the regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials;
- we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials which are conducted at multinational clinical facilities or in countries where the standard of care is potentially different from that of the U.S.;
- the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;
- we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates.

If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We initiated the ADVANCE Phase 1/2 trial in patients with A1AT deficiency in December 2017. Identifying and qualifying subjects to participate in the ADVANCE trial and future planned clinical trials for ADVM-053 and ADVM-022 will be critical to our success. The timing of future clinical trials will depend on the speed at which we can recruit subjects to participate in future testing of these product candidates.

Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. We will be required to identify and enroll a sufficient number of subjects with the relevant disease we are targeting for any future clinical trials for our product candidates. Potential subjects may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our trials. We also may encounter difficulties in identifying and enrolling subjects with a stage of disease appropriate for such future clinical trials. We may not be able to identify, recruit and enroll a sufficient number of subjects, or those with required or desired characteristics to achieve diversity in a study.

In particular, ADVM-043 and ADVM-053 are designed to treat rare genetic disorders with limited patient pools from which to draw for clinical trials. ADVM-043 is focused on the treatment of patients with A1AT deficiency. It is estimated that A1AT deficiency affects approximately 100,000 individuals in the U.S.

ADVM-053 is focused on the treatment of patients with HAE. The prevalence of HAE is estimated to be 1 in 10,000 to 1 in 50,000, impacting approximately 8,000 individuals in the United States. Enrollment of eligible subjects with orphan diseases like A1AT and HAE may be limited or slower than we anticipate in light of the small subject populations involved. We plan to seek initial marketing approval of these product candidates in the U.S. and Europe and we may not be able to initiate clinical trials if we cannot enroll a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or the EMA or other regulatory agencies. In addition, the process of finding and diagnosing subjects may prove costly.

Further, if patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or inadequate results in our preclinical studies or clinical trials or for other reasons, including competitive clinical trials for similar patient populations or available approved therapies, our recruitment of subjects, conduct of preclinical studies or clinical trials and ability to obtain regulatory approval of our product candidates may be hindered.

Trials using early versions of retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events. For example, generalized public backlash developed against gene therapy following the death in September 1999 of an 18-year-old who had volunteered for a gene therapy experiment at the University of Pennsylvania. Researchers at the university had infused the volunteer's liver with a gene aimed at reversing a rare metabolic disease of the liver. The procedure triggered an extreme immune-system reaction that caused multiple-organ failure in a very short time, leading to the first death to occur as a direct result of a gene therapy experiment. In addition, in 2003, 20 subjects treated for X-linked severe combined immunodeficiency in two gene therapy studies using a murine gamma-retroviral vector showed correction of the disease, but the studies were terminated after five subjects developed leukemia (four of whom were subsequently cured). The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer (often leukemia). Using molecular diagnostic techniques, it was determined that clones from these subjects showed retrovirus insertion in proximity to the promoter of the LMO2 proto-oncogene. Earlier generation retroviruses like the one used in these two trials have been shown to preferentially integrate in regulatory regions of genes that control cell growth.

If we have difficulty enrolling a sufficient number of patients to conduct clinical trials on our product candidates as planned, we may need to delay, limit or terminate future clinical trials, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We believe we have appropriately accounted for the above factors in our trials when determining expected clinical trial timelines, but we cannot assure you that our assumptions are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

The occurrence of serious complications or side effects in connection with use of our product candidates, either in preclinical studies or clinical trials or post-approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business, prospects, financial condition and results of operations.

During the conduct of preclinical studies and clinical trials, subjects may experience changes in their health, including illnesses, injuries and discomforts. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Various illnesses, injuries, and discomforts may be reported from time-to-time in clinical trials of our product candidates. It is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, financial condition and results of operations.

Our product candidates built on AAV vectors have similar risks to other gene therapy vectors, including inflammation, cytotoxic T-cell response, anti-AAV antibodies and immune response to the expressed transgene, such as T-cell responses and/or auto-antibodies against the expressed protein. Recent studies by third parties have also found that intravenous delivery of certain AAV vectors at very high doses may result in toxicity and that studies involving high doses of AAV vectors should be monitored carefully for such toxicity. In addition, patients given infusions of any protein may develop severe hypersensitivity reactions or infusion reactions. With respect to our product candidates that are being or may be studied in diseases of the eye, there are additional potential serious complications related to intravitreal injection to the eye. Serious complications or serious, unexpected side effects in connection with the use of our product candidates could materially harm our business, prospects, financial condition and results of operations.

Serious complications or serious, unexpected side effects in connection with the use of our product candidates could materially harm our business, prospects, financial condition and results of operations.

Risks Related to Our Reliance on Third Parties

We will rely on third parties to conduct our planned clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We are dependent on third parties to conduct preclinical studies and clinical trials for our product candidates, and, therefore, the timing of the initiation and completion of these studies or trials is controlled by such third parties and may occur at times substantially different from our estimates. Specifically, we use clinical research organizations ("CROs") to conduct our clinical trials and we rely on medical institutions, clinical investigators, CROs and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data.

There is no guarantee that any CROs, investigators or other third parties on which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, fails to meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit to the FDA. Any such delay or rejection could prevent us from commercializing our product candidates.

We have relied, and expect to continue to rely, on third parties to conduct some or all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. If any of these third parties on which we rely do not perform satisfactorily, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols.

These third parties may not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols. For example, on December 6, 2016, we delivered a notice to the appropriate persons at Cornell University of our intent to terminate our Amended and Restated Master Services Agreement for breach as a result of Cornell University's failure to deliver suitable materials for use in our clinical trials of ADVM-043. If third parties breach their contractual obligations to us, we may not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future IND submissions, development work, and approval of our product candidates.

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

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products.

We and our contract manufacturers are subject to significant regulation with respect to manufacturing our products. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and may have limited capacity.

We currently have relationships with limited number of suppliers for the manufacturing of our viral vectors and product candidates. Our suppliers may require licenses to manufacture such components if such processes are not owned by the suppliers or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities. All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturer for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with the FDA's current Good Manufacturing Practices ("cGMP"). These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current Good Laboratory Practice regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Our contract manufacturers have not produced a commercially-approved product and therefore have not obtained the requisite FDA approvals to do so. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect our manufacturing facilities or those of our third-party contractors involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If the facility does not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Such violations could also result in civil and/or criminal penalties. Any such remedial measures or other civil and/or criminal penalties imposed upon us or third parties with whom we contract could materially harm our business.

If we or our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, revocation of a pre-existing approval, other civil or criminal penalties or closing one or more manufacturing facilities. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

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 independent 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, financial conditions, results of operations and prospects.

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

Risks Related to Commercialization of Our Product Candidates

Any termination or suspension of, or delays in the commencement or completion of, clinical trials for our product candidates could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials in the U.S. for our product candidates, we need to submit the results of preclinical testing to the FDA, along with other information including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND. We may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our plans for our clinical trials. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA may require us to conduct additional preclinical

testing for any product candidate before it allows us to initiate clinical testing under any IND, which may lead to additional delays and increase the costs of our preclinical development. Delays with any regulatory body or agency may significantly affect our product development timeline. Delays in the commencement or completion of any clinical trials that we plan for our product candidates could significantly affect our product development costs. We do not know whether any trials that we plan will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA failing to grant permission to proceed or placing the clinical trial on hold;
- subjects failing to enroll or remain in our trial at the rate we expect;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- a facility manufacturing any of our product candidates or any of their components being ordered by the FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of cGMP or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practice or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;
- inspections of clinical trial sites by the FDA or the finding of regulatory violations by the FDA or an IRB that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire trial or that prohibit us from using some or all of the data in support of our marketing applications;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of any of our product candidates, or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of our clinical trials, or if we, the FDA or other regulatory authorities, the IRB, other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for a product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. If we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of, or the availability of data from, scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones will be based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline.

Final marketing approval for our product candidates by the FDA or other regulatory authorities for commercial use may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenue.

After the completion of our clinical trials and, assuming the results of the trials are successful, the submission of a BLA, we cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates, and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize our product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for our product candidates. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. If marketing approval for any product candidate is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

Even if we obtain marketing approval for any of our product candidates, they could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses, marketing or distribution or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. Following approval, if at all, of any of our product candidates, such candidate will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for any product candidate that may receive regulatory approval fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product or request us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue. The FDA has the authority to require a risk evaluation and mitigation strategy plan as part of a BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry.

In addition, if any of our product candidates is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. 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 sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Even if we receive regulatory approval we still may not be able to successfully commercialize any of our product candidates, and the revenue that we generate from its sales, if any, could be limited.

Even if any of our product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payers or the medical community. Coverage and reimbursement of our product candidates by third-party payers, including government payers, is also generally necessary for commercial success. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of new therapeutic options by health care providers and their patients;
- the prevalence and severity of any adverse effects;
- new procedures or methods of treatment that may be more effective in treating or may reduce the incidences of wAMD, A1AT deficiency, HAE or other conditions for which our products are intended to treat;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain and maintain sufficient third-party coverage and reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payers;
- unfavorable publicity relating to the product candidate; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage and reimbursement.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payers or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payers on the benefits of such a product candidate may require significant resources and may never be successful. In addition, our ability to successfully commercialize any of our product candidates will depend on our ability to manufacture our products, differentiate our products from competing products and defend and enforce our intellectual property rights relating to our products.

If the market for the treatment of wAMD is smaller than we believe it is, our future revenue may be adversely affected, and our business may suffer.

We are advancing the development of ADVM-022 for the treatment of wAMD, a disease we believe to be the most common cause of vision loss in adults over the age of 50 in developed countries. If the size of the market for wAMD is smaller than we anticipate, we may not be able to achieve profitability and growth. Our projections of the number of people who have wAMD, as well as the subset of people with these diseases who have the potential to benefit from treatment with wAMD, are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations and market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business.

Because the target patient populations of ADVM-043 and ADVM-053 are relatively small, we must be able to successfully identify patients and achieve a significant market share to maintain profitability and growth. If the market opportunities for these product candidates are smaller than we believe they are, our future revenue may be adversely affected, and our business may suffer.

ADVM-043 and ADVM-053 are designed to treat rare genetic diseases. ADVM-043 is designed to treat A1AT deficiency, which impacts approximately 100,000 individuals in the U.S. ADVM-053 is designed to treat HAE, which impacts approximately 8,000 individuals in the U.S. Our estimates of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with these product candidates, may prove to be incorrect. The number of patients in the U.S. and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with these products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Additionally, because the target patient populations for these product candidates are relatively small, the pricing and reimbursement of these product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell these product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to these product candidates (e.g., for administration of such product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell these products.

We may be unable to obtain orphan drug designation or exclusivity for ADVM-043, ADVM-053 or certain of our other product candidates. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the U.S. and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an orphan drug if it is intended to treat a rare disease or condition, which is defined under the Food, Drug and Cosmetic Act as having a patient population of fewer than 200,000 individuals in the U.S., or a patient population greater than 200,000 in the U.S. where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the European Union, following the opinion of the EMA's Committee for Orphan Medicinal Products, the European Commission grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the European Commission from approving another marketing application for a product that constitutes the same drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the U.S. and 10 years in the European Union. The exclusivity period in the U.S. can be extended by six months if the BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

We intend to request orphan drug designation for ADVM-043, ADVM-053 or any of our other product candidates that we believe could qualify, but there can be no assurances that the FDA or the European Commission will grant any of such requests. Additionally, the designation of any of our product candidates as an orphan product does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the U.S., even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug as the first or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care as compared to the first. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

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

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payers for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payer may depend upon a number of factors including the third-party payer's determination that use of a product candidate 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 candidate from a government or other third-party payer is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of the applicable product candidate to the payer. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. While there is no uniform coverage and reimbursement policy among payers in the United States, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, reimbursement amounts may reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved.

A number of gene therapy products have been approved over the past year by the FDA. Although the U.S. Center for Medicare & Medicaid Services ("CMS") subsequently approved its first method of coverage and reimbursement for one such product, the methodology has been subject to challenge by members of Congress. CMS's decision as to coverage and reimbursement for one product does not mean that all similar products will be eligible for analogous coverage and reimbursement. As there is no uniform policy for coverage and reimbursement amongst third-party payors in the United States, even if CMS approves coverage and reimbursement for any of our product candidates, it is unclear what affect, if any, such a decision will have on our ability to obtain and maintain coverage and adequate reimbursement from other private payors.

As a result of legislative proposals and the trend toward managed health care in the U.S., third-party payers are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. By way of example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively referred to as the Affordable Care Act, was enacted with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care organizations and established annual fees and taxes on manufacturers of certain prescription drugs.

Some of the provisions of the Affordable Care Act have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay, circumvent or loosen the implementation of certain provisions requirements mandated by the Affordable Care Act or otherwise circumvent some of the requirements for health insurance mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 23, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain Affordable Care Act-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Congress may consider other legislation to repeal or replace elements of the Affordable Care Act.

Other legislative changes have also been proposed and adopted in the U.S. since the Affordable Care Act 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 included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken.

These cost reduction initiatives could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business. We expect that additional healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our products, if approved, or additional pricing pressures.

Recently there has been heightened governmental scrutiny over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level,

Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological 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.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of health care may adversely affect:

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

Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

Our product candidates are designed to provide potential therapeutic benefit after a single administration and, therefore, the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

We are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products. The process of manufacturing our products is complex, highly regulated and subject to several risks, including:

- The manufacturing of biologics is extremely susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment or vendor or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing facility in which our products are made, such manufacturing facility may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facilities in which our products are made could be adversely affected by equipment failures, labor shortages, contaminants, raw materials shortages, natural disasters, power failures and numerous other factors.
- We and our contract manufacturers must comply with the FDA's cGMP regulations and guidelines. We and our contract manufacturers may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our contract manufacturers are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or any delay, interruption or other issues that arise in the manufacture, fill-finish, packaging or storage of our products as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products. This may lead to significant delays in the availability of products for our clinical trials or the termination or hold on a clinical trial, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could be costly and damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our products and/or may be subject to product recalls, seizures, injunctions or criminal prosecution.
- Our product candidates are biologics and require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be adequately characterized prior to manufacturing the final product. As a result, an assay of the finished product is not sufficient to ensure that the product will perform in the intended manner. Accordingly, we expect to employ multiple steps to attempt to control our manufacturing process to assure that the process works and the product or product candidate is made strictly and consistently in compliance with the process.
- Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory.
- Some of the raw materials required in our manufacturing process are derived from biological sources. Such raw materials are difficult to procure and may also be subject to contamination or recall. A material shortage, contamination, recall or

restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt commercialization.

- Any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. We may encounter problems achieving adequate or clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

We may not be successful in establishing and maintaining development or other strategic collaborations, which could adversely affect our ability to develop and commercialize product candidates and receive potential milestone payments.

We have entered into development or other strategic collaborations with major biotechnology or pharmaceutical companies. For example, our research collaboration and license agreement with Regeneron, which was announced in May 2014, covers up to eight distinct therapeutic targets, in which we could earn up to $80.0 million in development and regulatory milestones for product candidates directed toward each therapeutic target, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits. Additionally, in August 2016, we entered into a collaboration, option and license agreement with Editas Medicine, pursuant to which we and Editas will collaborate on certain studies using AAV vectors in connection with Editas' genome editing technology and we will grant to Editas an exclusive option to obtain certain exclusive rights to use our proprietary vectors in up to five ophthalmic indications. If Editas elects to develop a product using certain of our proprietary vectors, we will be eligible to receive up to $5.5 million in development milestone payments and $10.0 million in commercialization milestone payments for such product, and tiered royalties between the mid-single digits and low teens on net sales of such product, subject to certain adjustments.

Research activities under our collaboration agreements are subject to mutually agreed-on research plans and budgets, and if we and our strategic partners are unable to agree on the research plan or research budget in a timely fashion or at all, performance of research activities will be delayed. In addition, some of our strategic partners may terminate any agreements they enter into with us or allow such agreements to expire by their terms. Furthermore, our strategic partners have negotiated 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.

Moreover, if we fail to maintain development or other strategic collaborations related to our product candidates that we may choose to enter into:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly, and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development of any such product candidates.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of our product candidates. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because third parties may view the risk of failure in future clinical trials as too significant or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such development partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are disappointing. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market.

If our competitors develop treatments for the target indications of our product candidates that are approved more quickly than ours, marketed more successfully or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

We operate in highly competitive segments of the biopharmaceutical markets. We face competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical, biotechnology and gene therapy companies, as well as from academic institutions, government agencies and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies as well as with new treatments that may be introduced by our competitors. There are a variety of drug candidates and gene therapies in development or being commercialized by our competitors for the indications that we intend to test. Many of our competitors have significantly greater financial, product candidate development, manufacturing and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. In addition, universities and private and public research institutes may be active in our target disease areas, and some could be in direct competition with us. We also may compete with these organizations to recruit management, scientists and clinical development personnel. We will also face competition from these third parties in establishing clinical trial sites, registering subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

New developments, including the development of other biotechnology and vectorology technologies and methods of treating disease, occur in the pharmaceutical, biotechnology and gene therapy industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. Competition in drug development is intense. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available.

Even if we obtain regulatory approval for our product candidates, the availability and price of our competitors' products could limit the demand, and the price we are able to charge, for our product candidates. For example, EYLEA is currently available in the U.S. for treatment of wAMD and macular edema following central retinal vein occlusion ("CRVO"), and in the United Kingdom, Germany, Switzerland, Australia, Japan and certain other countries for the treatment of wAMD. Additionally, marketing approval has been obtained in the EU for EYLEA for the treatment of visual impairment due to macular edema secondary to CRVO. We will not achieve our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances. Our inability to compete with existing or subsequently introduced drug products or other therapies would have a material adverse impact on our business, prospects, financial condition and results of operations.

Our potential competitors in these diseases may be developing novel immune modulating therapies that may be safer or more effective than our product candidates, including ADVM-022. For example, if we continue clinical development of, and seek to commercialize, ADVM-022, it will compete with a variety of therapies currently marketed and in development for wAMD, using therapeutic modalities such as biologics, small molecules and gene therapy. Lucentis, EYLEA and Avastin are anti-VEGF therapies that are well established and widely accepted by physicians, patients and third-party payers as the standard of care for the treatment of wAMD. There are several other companies with marketed products or products in development for the treatment of wAMD, including Alcon, Allergan, Allegro Ophthalmics, LLC, Apellis Pharmaceuticals, Applied Genetic Technologies Corporation, Bayer, Hoffmann-La Roche Ltd., Iconic Therapeutics, Inc., Neurotech Pharmaceuticals, Inc., Novartis, Ocular Therapeutix, Inc., Ohr Pharmaceuticals, Inc., Ophthotech Corporation, Opthea Ltd., PanOptica Pharma, Genentech, SciFluor Life Science, LLC, Regeneron Pharmaceuticals, Inc., REGENXBIO Biosciences LLC, and Valeant Pharmaceuticals North America LLC.

For the treatment of A1AT deficiency and HAE, we know of a number of products currently in development that aim to reduce the frequency of injection, improve the route of administration, and deliver better efficacy compared to the standard-of-care treatments available today. There are several companies with products for A1AT deficiency in clinical development, including Applied Genetic Technologies Corporation and Kamada Ltd. For the treatment of HAE, there are several companies with products in clinical development, including CSL Behring, Biocryst Pharmaceuticals Inc., Ionis Pharmaceuticals, Inc., and Shire.

We have no sales, marketing or distribution capabilities, and we may have to invest significant resources to develop these capabilities.

We have no internal sales, marketing or distribution capabilities. If any of our product candidates ultimately receive regulatory approval, we may not be able to effectively market and distribute the product candidate. We may have to invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that any of our product candidates will be approved, if at all. We may not be able to hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms or at all. Even if we determine to perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by any product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our product candidates in both the U.S. and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product candidates. In some foreign countries, particularly in 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 the receipt of marketing approval for a product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Risks Related to Our Business Operations

Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of our product candidates or adversely affect our ability to conduct our business or obtain marketing approvals for our product candidates.

Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing symptomatic treatments they are already familiar with and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. Although none of our current product candidates utilize the gamma-retroviruses used in the 2003 studies, our product candidates do use a viral vector delivery system. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our future clinical trials. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

Adverse events in trials or studies conducted by us or other parties, in particular involving the same or similar AAVs to the ones we are using, even if not ultimately attributable to our product candidates, and resulting publicity, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any such adverse events occur, development and commercialization of our product candidates or advancement of any potential clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

We are dependent on the services of our key executives and scientific staff, and if we are not able to retain these members of our management or recruit additional management, clinical and scientific personnel, our business will suffer.

We are dependent on the principal members of our management and scientific staff. The loss of service of any of our management could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management, and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our development and commercialization efforts. Our success also depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. Our industry has experienced a high rate of turnover of management and scientific personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

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

We had 78 full-time employees as of February 28, 2018. We will need to grow our organization, or certain functions within our organization, substantially to continue development and pursue the potential commercialization of our product candidates, as well as function as a public company. As we seek to advance our product candidates, we may need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain or otherwise manage additional internal capabilities. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate any additional management, clinical and regulatory, financial, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to so accomplish could prevent us from successfully growing our company.

If we fail to comply with applicable state and federal healthcare laws, we may be subject to civil or criminal penalties and/or exclusion from federal and/or healthcare programs.

In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include anti-kickback, false claims, physician payment transparency and privacy and security laws and regulations. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced price items and services. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formula managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors 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 exemption or safe harbor. Many states have similar laws that apply to their state health care programs as well as private payers.

The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA") created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. The Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statute governing healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provided 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 False Claims Act.

Additionally, federal false claims laws and the civil monetary penalty law, including the False Claims Act, prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers, under the federal Physician Payments Sunshine Act, for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $0.2 million per year (or up to an aggregate of $1.0 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

In the course of conducting our business, we may also obtain individually identifiable patient health information including retinal scans from subjects participating in our clinical trials. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH"), imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information, upon certain health plans, healthcare clearinghouses and healthcare providers, and their respective business associates that perform services for them involving individually identifiable health information. In the event we are subject to HIPAA, and fail to properly maintain the privacy and security of certain individually identifiable health information, or we are responsible for an inadvertent disclosure or security breach of such individually identifiable health information, we could be subject to enforcement measures, including civil and criminal penalties and fines for violations of state and federal privacy or security standards, such as HIPAA and HITECH, and their respective implementing regulations. Additionally, certain states have adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. HIPAA, HITECH and comparable state laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. Any liability from failure to comply with the requirements of these laws, to the extent such requirements are deemed to apply to our operations, could adversely affect our financial condition. The costs of complying with privacy and security related legal and regulatory requirements are burdensome and could have a material adverse effect on our results of operations.

The need to build and maintain a robust compliance program with different compliance and/or reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, imprisonment, and additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results.

We and our development partners, third-party manufacturer and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and our development partners, third-party manufacturer and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our other 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 our product candidates. For example, we may be sued if our product candidates allegedly caused or cause injury or are 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 candidate, 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 or cease the 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 our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- 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 our product candidates; and
- a decline in our stock price.

We currently hold $5.0 million in product liability insurance, which may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Our inability 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 our product candidates. Although we plan to maintain such 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 will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may 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.

We and any of our future development partners will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we and any of our future development partners or CROs are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our future development partners report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our future development partners may fail to report adverse events we become aware of within the prescribed timeframe. We and any of our

future development partners may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we and any of our future development partners fail to comply with our or their reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, and seizure of our products or delay in approval or clearance of future products.

Our internal computer systems, or those of our development partners, CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

In the ordinary course of our business, we, our CROs, and other third parties on which we rely collect and store sensitive data, including legally protected patient health information, personally identifiable information about our employees, intellectual property, and proprietary business information. We manage and maintain our applications and data utilizing on-site systems. These applications and data encompass a wide variety of business critical information including research and development information and business and financial information.

The secure processing, storage, maintenance, and transmission of this critical information is vital to our operations and business strategy, and we devote significant resources to protecting such information. Despite the implementation of security measures to protect against unauthorized access or disclosure, our internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage or attacks from computer viruses, unauthorized access, breaches, interruptions due to employee error, malfeasance or other disruptions, lapses in compliance with privacy and security mandates, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, any such event could compromise our networks and the information stored there could be accessed by unauthorized parties, publicly disclosed, lost or stolen. We have measures in place that are designed to detect and respond to such security incidents and breaches of privacy and security mandates. Any such access, disclosure or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, such as the HIPAA, government enforcement actions and regulatory penalties. Unauthorized access, loss or dissemination could also disrupt our operations, including our ability to conduct research and development activities, process and prepare company financial information, manage various general and administrative aspects of our business and damage our reputation, any of which could adversely affect our business. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. In addition, there can be no assurance that we will promptly detect any such disruption or security breach, if at all. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

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

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 disclosure of unauthorized activities to us that violates: (1) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to regulatory authorities, (2) manufacturing standards, (3) federal and state health care fraud and abuse laws and regulations or (4) laws that require the reporting of financial information or data accurately. Specifically, sales, marketing, and business arrangements in the health care 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. Activities subject to these laws also involve improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks

or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Relating to Our Intellectual Property

Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies and universities.

We currently are heavily reliant upon licenses of certain patent rights and proprietary technology from third parties that are important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide adequate rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future, or may contain other limitations on our ability to use such intellectual property or technology. As a result, our ability to develop or commercialize our processes and product candidates may be limited by the terms of such agreements. In addition, we may not be able to prevent competitors from developing and commercializing competitive products to the extent our licenses to patents are non-exclusive or limited with respect to fields of use or territories.

Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition, results of operations and prospects.

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and their uses as well as our ability to operate without infringing upon the proprietary rights of others. There can be no assurance that any of our product candidates will have patent protection, that our patent applications or those of our licensors will result in patents being issued or that issued patents, if any, will afford sufficient protection against competitors with similar technology, nor is there any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our business, financial condition, results of operations and prospects.

Composition-of-matter patents on the biological or chemical 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. We cannot be certain that the claims in our patent applications covering composition-of-matter of any of our product candidates will be considered patentable by the U.S. Patent and Trademark Office ("USPTO") and courts in the U.S. or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged.

Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. However, methods of treating human diseases are considered unpatentable in many jurisdictions, and even where available this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;

- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the U.S. for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the U.S. may have patent laws less favorable to patentees than those upheld by the U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

In addition, we rely on the protection of our trade secrets and know-how. Although we have taken steps to protect our trade secrets and know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently.

Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands, especially in the field of gene therapy, and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of our product candidates. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

Although no third party has asserted a claim of patent infringement against us as of the date of this current report on Form 8-K, others may hold proprietary rights that could prevent our product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market our product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing our product candidates, which could harm our business, financial condition, results of operations and prospects.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control the prosecution and maintenance of the patents relating to our product candidates, there may be times when the filing and prosecution activities for platform technology patents that relate to our product candidates are controlled by our licensors. For example, we do not have the right to prosecute and maintain the patent rights licensed to us under agreements with Regents, Cornell University, and Virovek Corporation, and our ability to have input into such filing and prosecution activities is limited. If these licensors or any of our future licensors fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates or companion diagnostic, our ability to develop and commercialize those

product candidates and companion diagnostic may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged administratively or in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no 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 such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research and development programs, license necessary technology from third parties, or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

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. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act ("Leahy-Smith Act"), was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the U.S. transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and we may become involved in post-grant proceedings including opposition, derivation, reexamination, *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions 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 other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business, financial condition, results of operations and prospects could be materially and adversely affected.

We may fail to comply with any of our obligations under existing agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of our employees and consultants were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that our company, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. 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 or personnel, which could adversely impact our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

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 product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. 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 such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be materially harmed.

If we are able to secure FDA marketing approval for one of our product candidates that is covered by an issued U.S. patent, that patent may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Act"). The Hatch-Waxman Act permits 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, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial conditions and results of operations may be materially and adversely affected.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could materially and adversely impact our business, financial condition, results of operations, or prospects.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

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

Filing, prosecuting, obtaining and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S., or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the U.S. These products may compete with our product candidates, 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 foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, 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 jurisdictions 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.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapies that are similar to our product candidates but that are not covered by the claims of any patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- any patent applications that we have filed or may file in the future may not lead to issued patents;
- any of the issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where, or for products for which, we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, financial condition, results of operations and prospects.

Known third party patent rights could delay or otherwise adversely affect our planned development and sale of several of our lead programs.

We are aware of patent rights held by third parties that could be construed to cover certain aspects of our lead product candidates. A patent holder has the right to prevent others from making, using, or selling a drug that incorporates the patented compositions while the patent remains in force. While we believe that third party patent rights will not affect our planned development, regulatory clearance, and eventual marketing, commercial production, and sale of our product candidates, there can be no assurance that this will be the case. In each case, the relevant patent expires before we expect to commercially introduce such product candidate. In addition, the Hatch-Waxman exemption provided by U.S. patent law permits uses of compounds and biologics in clinical trials and for other purposes reasonably related to obtaining FDA clearance of drugs and biologics that will be sold only after patent expiration, so our use of our product candidates in those FDA-related activities does not infringe any patent holder's rights. However, were a patent holder to assert its rights against us before expiration of such patent holder's patent for activities unrelated to FDA clearance, the development and ultimate sale of our lead product candidates could be significantly delayed, and we could incur the expense of defending a patent infringement suit and potential liability for damages for periods prior to the patent's expiration.

Risks Related to Our Common Stock

If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to prepare accurate and timely consolidated financial statements being prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP") could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002 ("Sarbanes-Oxley"), our management is required to report upon the effectiveness of our internal control over financial reporting. When we lose our status as an "emerging growth company", unless we have become a smaller reporting company, our independent registered public accounting firm will also be required to attest to the effectiveness of our internal control over financial reporting, and the related report will also be required to be included in our annual reports filed with the SEC. However, for so long as we remain an emerging growth company, we intend to take advantage of an exemption available to companies meeting these criteria from these auditor attestation requirements. Sarbanes-Oxley Section 404 compliance requirements are complex and require significant documentation, testing, and possible remediation. If we (or our auditors if they are required to assess and attest to the effectiveness of our internal control over financial reporting) are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting, and the trading price of our common stock may decline.

Although we have determined that our internal control over financial reporting was effective as of December 31, 2017, we cannot assure you that there will not be material weaknesses in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The Nasdaq Stock Market, the SEC or other regulatory authorities. Failure to implement and maintain effective internal control over financial reporting, including failure to remediate any material weaknesses we or our auditors identify, could also restrict our future access to the capital markets.

The trading price of the shares of our common stock has been and could continue to be highly volatile, and purchasers of our common stock could incur substantial losses.

- Our stock price has been and is likely to continue to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including those discussed above and others such as:
- our plans regarding further development of ADVM-043, ADVM-053, or ADVM-022;
- our ability to enroll patients in any clinical trials that we plan in the future;
- our ability to obtain regulatory approvals for our product candidates and delays or failure to obtain such approvals;
- results of any clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory developments in the U.S. and foreign countries;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- failure to maintain our existing third party license and collaboration agreements;
- delays in manufacturing adequate supply of our product candidates;
- adverse publicity relating to the gene therapy market generally, including with respect to other products and potential products in such markets;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations;
- sales of our stock by insiders and stockholders;
- trading volume of our common stock;
- general economic, industry and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies following periods of volatility in the market prices of these companies' stock, and similar litigation has been instituted against us. Such litigation could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We and certain of our former officers have been named defendants in purported securities class action lawsuits. These, and any additional securities litigation, could result in substantial losses and may divert management's time and attention from our business.

On June 15, 2015, we announced the top-line results of our Phase 2a clinical trial for AVA-101. In July 2015, three purported securities class action lawsuits were commenced in the U.S. District Court for the Northern District of California, naming as defendants us and certain of our former officers. These lawsuits assert that the defendants violated the Securities Exchange Act of 1934, as amended ("Exchange Act"), and the Securities Act of 1933, as amended ("Securities Act"), and allege that the defendants made materially false and misleading statements and omitted allegedly material information related to, among other things, the Phase 2a clinical trial for AVA-101 and the prospects of AVA-101. The plaintiffs seek unspecified damages, attorneys' fees and other costs, each on behalf of a purported class of persons and entities who purchased or otherwise acquired our publicly traded securities between July 31, 2014 and June 15, 2015. It is possible that additional suits will be filed with respect to these same matters and also naming us and/or our officers and directors as defendants.

In addition, in December 2015, a putative securities class action lawsuit was filed against us, our board of directors, underwriters of our January 13, 2015, follow-on public stock offering, and two of our institutional stockholders, in the Superior Court of the State of California for the County of San Mateo. The complaint alleges that, in connection with our follow-on stock offering, the defendants violated the Securities Act by allegedly making materially false and misleading statements and by allegedly omitting material information related to the Phase 2a clinical trial for AVA-101 and the prospects of AVA-101. The complaint seeks unspecified compensatory and rescissory damages, attorneys' fees and other costs.

In March 2017, we reached an agreement to settle the asserted actions. The proposed aggregate amount of the settlement is $13.0 million, of which $1.0 million would be contributed by us to cover our indemnification obligations to the underwriters, and the remainder would be contributed by our insurers. Notice of the settlement was provided to stockholders in the fall of 2017, and no stockholder objected to the settlement. In January 2018, the San Mateo Superior Court entered a judgment and order finally approving the settlement and, in February 2018, the U.S. District Court dismissed the consolidated federal action with prejudice. If the settlement does not become effective and litigation resumes, following an appeal or otherwise, adverse outcomes in the actions could result in substantial damages. We and the defendants have denied and continue to deny each and all of the claims alleged in the actions, and the settlement does not assign or reflect any admission of fault, wrongdoing or liability as to any defendant. If final court approval is not obtained with respect to the settlement or the settlement otherwise does not become effective and litigation resumes, adverse outcomes in the actions could result in substantial damages.

The current securities litigation and any future litigation of this type could result in diversion of management's attention and resources, which could adversely impact our business. Monitoring and defending against legal actions is time-consuming for our management and detracts from our ability to focus fully on our business activities.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our clinical trial and development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting our product candidates;
- our execution of any collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- nature and terms of stock-based compensation grants; and
- derivative instruments recorded at fair value.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

If we sell shares of our common stock or securities convertible into or exercisable for shares of our common stock in future financings, licensing or collaboration arrangements, or acquisitions, or additional shares under our at-the-market sales agreement, stockholders may experience immediate dilution and, as a result, our stock price may decline.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, licensing, collaboration or similar arrangements, grants and debt financings. We do not have any committed external source of funds. As a result, we may from time to time issue additional shares of common stock or securities convertible into or exercisable for shares of our common stock. We filed a universal shelf registration statement on Form S-3 with the SEC, which was declared effective on August 22, 2017, pursuant to which we registered for sale up to $150.0 million of any combination of our common stock, preferred stock, debt securities, warrants, and/or units from time to time and at prices and on terms that we may determine, including up to $50.0 million of our common stock available for issuance pursuant to our sales agreement with Cowen. Pursuant to the sales agreement, we may offer and sell, from time to time at our discretion, shares of our common stock having an aggregate offering price of up to $50.0 million through Cowen as our sales agent. Under the sales agreement, Cowen may sell the shares by any method permitted by law deemed to be an "at the market" offering as defined in Rule 415 of the Securities Act. We may seek to raise additional capital at any time. Further, pursuant to the aforementioned universal shelf registration statement, in February 2018, we completed the issuance of 10,222,235 shares of our common stock at $6.75 per share in an underwritten public offering for net proceeds to us of approximately $64.3 million. 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 of these securities may include liquidation or other preferences that adversely affect your rights as a holder of our common stock. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends or other distributions. Furthermore, we may issue common stock as consideration in acquisitions. For example, in May 2016, we issued 14,087,246 shares of our common stock to Annapurna's shareholders as consideration for all of the outstanding shares of Annapurna. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

If we raise additional funds through licensing, collaboration or similar arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research and development programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult 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 bylaws may delay or prevent an acquisition of us or a change in our management. These provisions include:

- the authorization of the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- the limitation of the removal of directors by the stockholders;
- a staggered board of directors;
- the prohibition of stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- the elimination of the ability of stockholders to call a special meeting of stockholders;
- the ability of our board of directors to accelerate the vesting of outstanding option grants, restricted stock units or other equity awards upon certain transactions that result in a change of control; and
- the establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirers to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, 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, which is responsible for appointing the members of our management.

We do not intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

We are an emerging growth company, and the reduced reporting requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until the last day of the fiscal year 2019, although circumstances could cause us to lose that status earlier, including if we become a large accelerated filer (in which case we will cease to be an emerging company as of the date we become a large accelerated filer, which, generally, would occur if, at the end of a fiscal year, among other things, the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the last business day of our most recently completed second fiscal quarter), if we have total annual gross revenue of $1.0 billion or more during any fiscal year (in which cases we would no longer be an emerging growth company as of December 31 of such fiscal year), or if we issue more than $1.0 billion in non-convertible debt during any three year period before that time (in which case 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," which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley and reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may 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.

We have incurred and will continue to incur significant increased costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business, results of operations and financial condition. In addition, Sarbanes-Oxley, as well as rules adopted by the SEC and The Nasdaq Global Market that implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC adopted additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

The rules and regulations applicable to public companies have substantially increased our legal and financial compliance costs and make some activities more time-consuming and costly. To the extent these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations and prospects. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

The recently passed comprehensive tax reform bill could adversely affect our business, results of operations and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended (the "Code"). The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including adoption of a flat 21% corporate tax rate, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction of net operating losses generated in tax years beginning after December 31, 2017 to 80% of taxable income and elimination of carrybacks of such net operating losses, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, current inclusion in U.S. federal taxable income of certain earnings of controlled foreign corporations for tax years beginning after January 1, 2018, mandatory capitalization of research and development expenses beginning in 2022, immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions generally referred to as "orphan drugs"). Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain, and our business, results of operations and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our ability to use net operating loss carryforwards and other tax attributes may be limited by the Code.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. As of December 31, 2017, we had U.S. federal net operating loss ("NOL") carryforwards of approximately $53.2 million to offset future federal income. NOLs expire at various years beginning with 2036. As of December 31, 2017, we also had U.S. state NOL carryforwards of approximately $37.8 million to offset future state income. U.S. State NOLs expire at various years beginning with 2036. At December 31, 2017, we also had approximately $44.1 million of foreign net operating loss carryforwards which may be available to offset future foreign income; these carryforwards do not expire.

Under the newly enacted federal income tax law, federal NOLs incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating NOLs is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Code, our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we experience an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. In connection with our acquisition of Annapurna in May 2016, we determined that certain NOLs for both federal and state purposes were severely limited and therefore we removed a significant amount of NOLs from our deferred tax assets. In addition, we may have experienced an ownership change as a result of the February 2018 underwritten public offering of our common stock, and may in the future experience ownership changes future offerings or other changes in the ownership of our stock. As a result, the amount of the NOLs and research and credit carryforwards presented in our financial statements could be limited and may expire unutilized.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our corporate headquarters are located in Menlo Park, California, where we lease and occupy approximately 36,000 square feet of office space. The current term of our lease expires on May 8, 2020, with an option to extend the term through May 8, 2024. We believe that our existing facilities are adequate for our current needs. When our lease expires, we may exercise our renewal option or look for additional or alternate space for our operations and we believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

In July 2015, three securities class action lawsuits were filed against us and certain of our officers in the U.S. District Court for the Northern District of California ("U.S. District Court"), each on behalf of a purported class of persons and entities who purchased or otherwise acquired our publicly traded securities between July 31, 2014 and June 15, 2015. The lawsuits assert claims under the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Securities Act of 1933, as amended (the "Securities Act") and allege that the defendants made materially false and misleading statements and omitted allegedly material information related to, among other things, the Phase 2a clinical trial for AVA-101, a product candidate which is no longer being developed, and the prospects of AVA-101. The complaints seek unspecified damages, attorneys' fees and other costs.

In December 2015, a putative securities class action lawsuit was filed against us, our board of directors, underwriters of our January 13, 2015, follow-on public stock offering, and two of our institutional stockholders, in the Superior Court of the State of California for the County of San Mateo ("San Mateo Superior Court"). The complaint alleges that, in connection with our follow-on stock offering, the defendants violated the Securities Act by allegedly making materially false and misleading statements and by allegedly omitting material information related to the Phase 2a clinical trial for AVA- 101 and the prospects of AVA-101. The complaint seeks unspecified compensatory and rescissory damages, attorneys' fees and other costs. The plaintiff has dismissed the two institutional stockholder defendants.

On March 16, 2017, we reached an agreement to settle the asserted actions. The proposed aggregate amount of the settlement is $13.0 million, of which $1.0 million would be contributed by us to cover our indemnification obligations to the underwriters, and the remainder would be contributed by our insurers. We and the defendants have denied and continue to deny each and all of the claims alleged in the actions, and the settlement does not assign or reflect any admission of fault, wrongdoing or liability as to any defendant. Notice of the settlement was provided to shareholders in the fall of 2017, and no shareholder objected to the settlement. On January, 19, 2018, the San Mateo Superior Court entered a judgment and order finally approving the settlement. And on February 5, 2018, the U.S. District Court entered an order dismissing the consolidated federal action with prejudice. If the settlement does not become effective and litigation resumes, following an appeal or otherwise, adverse outcomes in the actions could result in substantial damages. We recorded $1.0 million as general and administrative expense during the three months ended March 31, 2017, when the amount and time of settlement became estimable and probable.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Our common stock has been listed on The Nasdaq Global Market since July 31, 2014, and is currently listed under the symbol "ADVM". Prior to July 31, 2014, there was no public trading market for our common stock. The following table sets forth for the periods indicated the high and low closing prices per share of our common stock as reported on The Nasdaq Global Market:

Year ended December 31, 2017	High	Low
First Quarter	$ 3.35	$ 2.55
Second Quarter	$ 3.10	$ 2.50
Third Quarter	$ 3.65	$ 2.45
Fourth Quarter	$ 3.95	$ 2.85

Year ended December 31, 2016	High	Low
First Quarter	$ 8.80	$ 4.15
Second Quarter	$ 6.24	$ 3.02
Third Quarter	$ 4.76	$ 3.04
Fourth Quarter	$ 4.35	$ 2.80

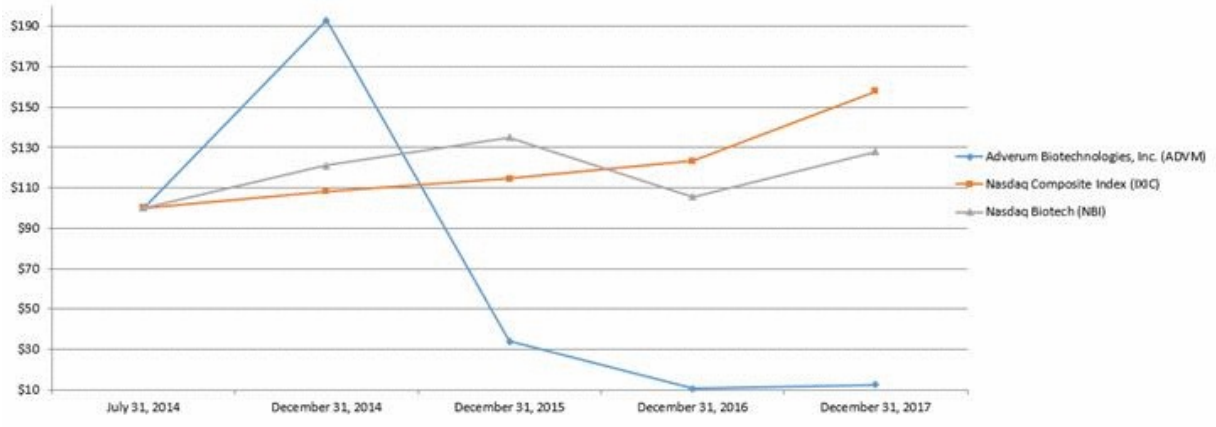
As of February 28, 2018, we had approximately 19 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return of an investment of $100 in cash on July 31, 2014, which is the date our common stock first began trading on the Nasdaq Global Market, through December 31, 2017 for (i) our common stock, (ii) the Nasdaq Composite Index and (iii) the Nasdaq Biotech Index. Pursuant to applicable SEC rules, all values assume reinvestment of the full amount of all dividends, however no dividends have been declared on our common stock to date. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



$100 investment in stock or index	July 31, 2014	December 31, 2014	December 31, 2015	December 31, 2016	December 31, 2017
Adverum Biotechnologies, Inc. (ADVM)	$ 100.00	$ 192.93	$ 34.01	$ 10.36	$ 12.50
Nasdaq Composite Index (IXIC)	$ 100.00	$ 108.38	$ 114.58	$ 123.19	$ 157.98
Nasdaq Biotech (NBI)	$ 100.00	$ 121.12	$ 134.95	$ 105.69	$ 127.94

Recent Sales of Unregistered Securities

None.

Use of Proceeds

On August 5, 2014, we closed our IPO and issued 6,900,000 shares of our common stock at an initial offering price of $17.00 per share. The offer and sale of all of the shares in the IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File Nos. 333-197133 and 333-197739), which was declared effective by the SEC on July 30, 2014. The joint book-running managers for the IPO were Jefferies LLC, Cowen and Company, LLC and Piper Jaffray & Co. The aggregate offering price to the public for the shares sold in the IPO was $117.3 million. We received net proceeds from the IPO of approximately $106.5 million, after deducting underwriting discounts and commissions of approximately $8.2 million and expenses of approximately $2.6 million payable by us. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates.

We have discontinued development of AVA-101, and so we will not use approximately $20.0 million of our net proceeds from the IPO to fund Phase 3 research and development startup activities for our AVA-101 study, as we had described in our final prospectus filed with the SEC on July 31, 2014 pursuant to Rule 424(b) of the Securities Act. Instead, we have reallocated such proceeds to fund research and development expenses for additional preclinical studies relating to our wAMD gene therapies, ADVM-022 and ADVM-032 and for ADVM-043 for A1AT deficiency and for ADVM-053 for HAE.

Subsequent Stock Offerings

On January 13, 2015, we completed a follow-on offering of 2,369,375 shares of our common stock, which included 359,918 shares we issued pursuant to the underwriters' exercise of their option to purchase additional shares, and we received net proceeds of approximately $130.6 million, after underwriting discounts, commissions and offering expenses.

In March 2015, (i) we received net proceeds of approximately $8.3 million, after discounts and other issuance costs, which resulted from the sale of 230,000 common shares, and (ii) we issued 230,000 common shares to a stockholder that exercised warrants prior to the IPO.

In August 2017, we entered into an at-the-market sales agreement with an agent for the sales of our common stock at market price (the "2017 stock offering agreement"). Under the terms and conditions of the 2017 stock offering agreement, we may offer to sell our common stock for an aggregate offering price of up to $50.0 million through the agent from time to time. In January 2018, we sold a total of 1,419,893 shares of our common stock at market prices under the 2017 stock offering agreement and raised total net proceeds of $5.7 million, net of issuance costs. We have sold a total of 6,550,232 shares of our common stock at market prices pursuant to the 2017 stock offering agreement and have raised total net proceeds of approximately $22.5 million, net of issuance costs.

In February 2018, we completed an underwritten offering for the sale of 10,222,235 shares of our common stock and raised total net proceeds of approximately $64.3 million, after discounts and other issuance costs.

We invested the funds received in short-term, interest-bearing investment-grade securities and government securities.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Item 6. Selected Financial Data

The following selected consolidated financial data should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations", the consolidated financial statements and related notes, and other financial information included in this Annual Report on Form 10-K.

We derived the consolidated financial data for the years ended December 31, 2017, 2016 and 2015 and as of December 31, 2017 and 2016 from our consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. The consolidated financial data for the years ended December 31, 2014 and 2013 and as of December 31, 2015, 2014 and 2013 are derived from our audited consolidated financial statements which are not included in this Annual Report on Form 10-K. Historical results are not necessarily indicative of the results to be expected in future periods.

	Years ended December 31,				
	2017	2016	2015	2014	2013
(In thousands, except per share data)					
Consolidated Statements of Operations and Comprehensive Loss Data:					
Revenue					
Collaboration and license revenue	$ 1,849	$ 1,455	$ 2,319	$ 572	$ —
Government grant revenue		—	—	—	480
Operating expenses:					
Research and development (1)	39,839	31,670	25,462	16,976	2,151
General and administrative (2)	20,857	24,355	22,107	7,998	1,783
Impairment of goodwill and intangible assets (3)	—	60,714	—	—	—
Restructuring charges (4)	—	—	2,573	—	—
Total operating expenses	60,696	116,739	50,142	24,974	3,934
Operating loss	(58,847)	(115,284)	(47,823)	(24,402)	(3,454)
Other income (expense)					
Interest expense	—	—	—	(18)	(73)
Other income (expense), net	2,700	762	370	(21)	(4)
Changes in fair value of embedded derivative	—	—	—	—	18
Changes in fair value of warrant liabilities	—	—	—	(759)	(92)
Loss on extinguishment of related-party convertible notes	—	—	—	(204)	(1,671)
Total other income (expense), net	2,700	762	370	(1,002)	(1,822)
Net loss before income tax benefit	(56,147)	(114,522)	(47,453)	(25,404)	(5,276)
Income tax benefit (5)	—	775	—	—	—
Net loss after income tax benefit	(56,147)	(113,747)	(47,453)	(25,404)	(5,276)
Deemed dividend (6)	—	—	—	(3,230)	—
Net loss attributable to common stockholders	$ (56,147)	$ (113,747)	$ (47,453)	$ (28,634)	$ (5,276)
Other comprehensive loss:					
Net unrealized loss on marketable securities	(182)	6	(6)	—	—
Foreign currency translation adjustment	(774)	(2)	(15)	(17)	19
Comprehensive loss	$ (57,103)	$ (113,743)	$ (47,474)	$ (25,421)	$ (5,257)
Net loss per share attributable to common stockholders-basic and diluted	$ (1.29)	$ (3.14)	$ (1.86)	$ (2.46)	$ (1.44)
Weighted-average common shares outstanding-basic and diluted	43,661	36,246	25,479	11,651	3,673

(1) During the year ended December 31, 2016, we recorded approximately $1.4 million of one-time stock-based compensation charge in connection with the separation agreement with a certain executive officer.

(2) During the year ended December 31, 2015, we recorded approximately $2.4 million of one-time stock-based compensation expense in connection with the termination of a certain executive officer. During the year ended December 31, 2016, we recorded approximately $1.5 million of one-time stock-based compensation charges in connection with the separation agreements with our certain executive officers.

(3) During the year ended December 31, 2016, we recorded $49.5 million of goodwill impairment charge related to our goodwill impairment analysis. Additionally, we performed our annual impairment assessment of our in-process research and development intangible assets in the fourth quarter of 2016 and recorded $11.2 million of intangible impairment charge during the year ended December 31, 2016.

(4) During the year ended December 31, 2015, we recorded a total of $2.6 million restructuring charges related to one-time termination severance payments and other employee-related benefits, including approximately $1.0 million of stock-based compensation expense related to the acceleration of stock awards.

(5) During the year ended December 31, 2016, we recorded income tax benefit of $0.8 million related to the change in the deferred tax liabilities balances due to the impairment of our intangible assets.

(6) In April 2014, we repurchased 531,208 shares of Series A convertible preferred stock for $4.0 million. The difference between the repurchase price of $7.53 per share and original issuance price of $1.45 per share was recorded as a deemed dividend of $3.2 million to a preferred stockholder and effected the calculation of net loss attributable to common stockholders and net loss per share for the year ended December 31, 2014.

	As of December 31,				
	2017	2016	2015	2014	2013
(In thousands)					
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 70,519	$ 222,170	$ 221,348	$ 159,404	$ 564
Short-term investments	119,966	—	37,732	—	—
Working capital	183,067	215,378	254,418	154,807	(340)
Total assets	201,905	234,583	264,319	161,906	1,085
Other non-current liabilities	481	386	—	—	—
Accumulated deficit	(254,062)	(197,915)	(84,168)	(36,715)	(8,869)
Total stockholders' equity (deficit)	184,028	215,600	252,592	149,483	(8,210)

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

You should read the following discussion of our financial condition and results of operations in conjunction with the financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed below and elsewhere in this Annual Report on Form 10-K, particularly in "Cautionary Note Regarding Forward-Looking Statements" and "Risk Factors."

Overview

Adverum is a clinical-stage gene therapy company targeting unmet medical needs in serious rare and ocular diseases. We are leveraging our next-generation adeno-associated virus ("AAV")-based directed evolution platform to generate gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. In May 2016, we closed our acquisition of Annapurna Therapeutics SAS ("Annapurna"), a privately-held French gene therapy company, (the "Annapurna acquisition"). Our core capabilities include clinical development, novel vector development, and in-house manufacturing expertise, specifically in process development, assay development and Good Manufacturing Practices quality control. Our leadership team has significant drug development and gene therapy expertise.

We are advancing our robust pipeline of gene therapy candidates designed to treat rare diseases alpha-1 antitrypsin ("A1AT") deficiency and hereditary angioedema ("HAE") as well as in wet age-related macular degeneration ("wAMD").

For the treatment of A1AT deficiency, we are advancing our gene therapy product candidate ADVM-043, AAVrh.10-A1AT, in an ongoing Phase 1/2 clinical trial (the "ADVANCE trial"). The ADVANCE trial is a multi-center, open-label, dose-escalation study. The primary endpoint is safety and tolerability and secondary endpoints include changes in plasma concentrations of both total and M-specific A1AT levels. The study will include up to 20 patients across up to four planned dosing cohorts of up to 5 patients each. The first three cohorts of patients will receive a single intravenous ("IV") administration of ADVM-043 and the fourth cohort of patients will receive a single intrapleural ("IP") administration of ADVM-043. In the first cohort, patients (n=2) have been dosed and evaluated following a single administration of ADVM-043 at a dose of ~1E12 vg/kg (8E13 total vg). Based on a review of the preliminary safety data, the independent data monitoring committee ("DMC") has recommended escalating to the intermediate dose (~5E12 vg/kg (4E14 total vg) of ADVM-043, which will be utilized in the second cohort of patients, which is open for enrollment. Further details about the study can be found at ClinicalTrials.gov under trial identifier number NCT02168686. We expect to report preliminary data from this trial in the second half of 2018.

For treatment of the rare disease HAE, we are advancing our preclinical gene therapy product candidate ADVM-053, AAVrh.10-C1EI. ADVM-053 is designed as a potential single-administration treatment to provide sustained release of the C1 esterase inhibitor ("C1EI") protein to eliminate protein level variability and prevent breakthrough attacks. In preclinical studies, a single IV administration of ADVM-053 increased C1EI protein expression above therapeutic levels and decreased vascular permeability. We plan to submit an Investigational New Drug ("IND") application for ADVM-053 for HAE with the U.S. Food and Drug Administration ("FDA") in the second half of 2018.

For wAMD, we are advancing our preclinical gene therapy product candidate ADVM-022, AAV.7m8-aflibercept. With a proprietary vector capsid ("AAV.7m8") and a proprietary expression cassette, ADVM-022 is administered as a single intravitreal injection and is designed to minimize the treatment burden of frequent injections, which is the current standard of care. We have presented preclinical proof-of-concept data of ADVM-022's anti-angiogenic effect in the laser-induced choroidal neovascularization ("CNV") model in non-human primates, the industry standard for testing new wAMD therapies. The data from a single injection of ADVM-022 showed efficacy that was comparable to the anti-Vascular Endothelial Growth Factor ("VEGF") standard of care, which was the positive control in the CNV model. At scientific meetings in September 2017, we presented additional long-term data, which continued to demonstrate sustained expression of anti-VEGF protein following a single intravitreal injection of ADVM-022. Pharmacokinetic data on one non-human primate demonstrated sustained expression for 52 weeks. In a separate ongoing study, sustained expression for at least seven months has been observed in seven non-human primates. In this ongoing preclinical study, we continue to assess the durability of protein expression in non-human primates and expect to report 12-month data in the first half of 2018. We plan to submit an IND application for ADVM-022 for wAMD with the FDA in the second half of 2018.

Our earlier-stage research programs include gene therapy product candidates targeting cardiomyopathy associated with Friedreich's ataxia ("FA") and severe allergy.

Our partnered programs include vectors we are developing under collaboration agreements. Under an agreement with Editas Medicine, Inc. ("Editas") we are leveraging our AAV-vectors for use with Editas' leading Clustered Regularly Interspaced Short Palindromic Repeats ("CRISPR")-based genome editing technologies to treat up to five inherited retinal diseases. Our agreement with Regeneron Pharmaceuticals, Inc. ("Regeneron") provides for development of up to eight distinct ocular therapeutic targets, four of which are already identified, including AVA-311 for the treatment of juvenile X-Linked Retinoschisis ("XLRS").

Financial Overview

Summary

We have not generated positive cash flow or net income from operations since our inception and, as of December 31, 2017, we had an accumulated deficit of $254.1 million. We expect to incur substantial expenses and increasing losses from operations in the foreseeable future as we continue our research and development efforts, advance our product candidates through preclinical and clinical development, manufacture clinical study materials, seek regulatory approval, and prepare for and, if approved, proceed to commercialization. We are at an early stage of development and may never be successful in developing or commercializing our product candidates.

While we may in the future generate revenue from a variety of sources, including license fees, milestone and research and development payments in connection with strategic partnerships, and potentially revenue from product sales if any of our product candidates are approved, to date we have not generated any revenue from product sales.

We entered into our collaboration and license arrangements with Regeneron in May 2014 and Editas in August 2016. Both arrangements are revenue-generating arrangements, refer to Note 7, *Significant Agreements*, of the notes to consolidated financial statements included in this Form 10-K for details. We have no clinical or commercial manufacturing facilities, and all of our clinical manufacturing activities are contracted out to third parties. Additionally, we use third-party clinical research organizations ("CROs") to carry out our clinical development and we do not have a sales organization.

We expect to incur substantial and increasing expenditures in the foreseeable future for the development and potential commercialization of our product candidates. We will need substantial additional funding in the future to support our operating activities as we advance our product candidates through preclinical and clinical development, seek regulatory approval and prepare for and, if approved, proceed to commercialization. Adequate funding may not be available to us on acceptable terms, or at all. If we are unable to raise capital, or to do so on acceptable terms, when needed, or to form additional collaboration partnerships to support our efforts, we could be forced to delay, reduce or eliminate our research and development programs or potential commercialization efforts.

As of December 31, 2017, we had $190.5 million in cash, cash equivalents and short-term investments. We believe that we have sufficient funds, together with the net proceeds from our February 2018 underwritten public offering of our common stock, to continue our operations through the end of 2019.

In August 2017, we entered into an at-the-market sales agreement with an agent for the sales of our common stock at market price (the "2017 stock offering agreement"). Under the terms and conditions of the 2017 stock offering agreement, we may offer to sell our common stock for an aggregate offering price of up to $50.0 million through the agent from time to time. In January 2018, we sold a total of 1,419,893 shares of our common stock at market prices under the 2017 stock offering agreement and raised total net proceeds of $5.7 million, net of issuance costs. We have sold a total of 6,550,232 shares of our common stock at market prices pursuant to the 2017 stock offering agreement and raised total net proceeds of approximately $22.5 million, net of issuance costs.

In February 2018, we completed an underwritten public offering for the sale of 10,222,235 shares of our common stock and raised total net proceeds of approximately $64.3 million, after discounts and other issuance costs.

Revenue

To date we have not generated any revenue from the sale of our products. We generate revenue through research, collaboration and license arrangements with our strategic partners. As of December 31, 2017, our total deferred revenue related to collaboration arrangements with our strategic partners was $7.1 million. We recognized $1.8 million, $1.5 million and $2.3 million of revenue associated with these collaboration arrangements during the years ended December 31, 2017, 2016 and 2015, respectively.

Agreement with Editas

In August 2016, we entered into a collaboration, option and license agreement with Editas. Under the terms of the agreement, we received $1.0 million non-refundable upfront payment, with $0.5 million of such payment to be credited against Editas' obligation to fund research and development costs. As the agreement provides for multiple deliverables, we accounted for this agreement as a multiple elements revenue arrangement. At the inception of the agreement, identified deliverables include research services, manufacturing of viral vectors for research, participation in the joint research committee and exclusivity during the option period. These deliverables did not appear to have a standalone value and were combined into one unit of accounting. Options for each indication to license our AAV vector are considered substantive options and do not include significant incremental discounts. Therefore, they are not considered as deliverables under the agreement. We allocated the $1.0 million received to a single unit of accounting identified in the arrangement. We recognize $1.0 million ratably over the associated period of performance, which is the maximum research period of three years. As there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, we recognize revenue on a straight-line basis.

In January 2018, we and Editas extended the collaboration, option and license agreement. In consideration for extending the agreement, Editas made a one-time payment to Adverum of $0.5 million in February 2018. Refer to Note 17 of the notes to consolidated financial statements included in this Form 10-K for details.

Agreement with Regeneron

In May 2014, we entered into a research, collaboration and license agreement with Regeneron. Under the terms of the agreement, we received initial payments of $8.0 million that included payment for research license fees, prepaid collaboration research costs and the right of first negotiation for a potential license to develop and commercialize AVA-101, a prior wAMD gene therapy that is no longer in development. As the agreement provides for multiple deliverables, we account for this agreement as a multiple elements revenue arrangement. If deliverables do not appear to have a standalone fair value, they were combined with other deliverables into a unit of accounting with standalone fair value. We allocated the $8.0 million received to the fair values of the two units of accounting identified in the arrangement. We recognize $6.5 million allocated to the first unit of accounting for research licenses and related research and development services ratably over the associated period of performance, which is the maximum research period of eight years. As there was no discernible pattern of performance and/or objectively measurable performance measures did not exist, revenue associated with the first unit of accounting is recognized on a straight-line basis over the eight-year performance period. The remaining $1.5 million allocated to the second unit of accounting for the time-limited right of first negotiation for AVA-101 was deferred. In November 2015, Regeneron notified us that it did not exercise its right of first negotiation and, as a result, we recognized the entire $1.5 million as revenue during the year ended December 31, 2015. In February 2017, Regeneron notified us that pursuant to the terms of the research, collaboration and license agreement, it extended the initial research term for an additional three years, through May 1, 2020.

The portion of the upfront payment that was applied to the original research budget was fully used in the fourth quarter of 2015, and we and Regeneron, through a joint review committee, agree annually on an updated research and development services budget through the research period. We invoice Regeneron quarterly for services performed in each prior quarter. These additional research fees are added to the research licenses and related research and development services unit of accounting, recorded as deferred revenue and recognized to revenue over the remaining maximum research term.

Under our research, collaboration and license agreement with Regeneron, we are required to have a mutually agreed-on research plan with Regeneron in order to invoice Regeneron for services performed. We do not currently have a research plan in place, and, consequently, we are not currently receiving any reimbursements from Regeneron.

Our ability to generate product revenue and become profitable depends upon our ability to successfully develop and commercialize our product candidates. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the amount or timing of product revenue. Even if we are able to generate revenue from the sale of our products, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Research and Development Expenses

Conducting a significant amount of research and development is central to our business model. Research and development expenses include primarily personnel-related costs, stock-based compensation expense, laboratory supplies, consulting costs, external contract research and development expenses, including expenses incurred under agreements with CROs, the cost of acquiring, developing and manufacturing clinical study materials, and overhead expenses, such as rent, equipment depreciation, insurance and utilities.

Research and development costs are expensed as incurred. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

We estimate preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. 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. We estimate the amounts incurred through communications with third party service providers and our estimates of accrued expenses as of each balance sheet date are based on information available at the time. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly.

At this time, we cannot reasonably estimate the nature, timing or aggregate costs of the efforts that will be necessary to complete the development of any of our product candidates. The successful development and commercialization of a product candidate is highly uncertain, and clinical development timelines, the probability of success, and development and commercialization costs can differ materially from expectations.

We received refundable tax credits from the Australian and French tax authorities in connection with certain research costs incurred by our subsidiary conducting research in Australia and France. These refunds do not depend on our taxable income or tax position and therefore we do not account for them under an income tax accounting model. We recognize such refunds as government grants in the period when qualified expenses are incurred as a reduction of research expenses. We have recorded the reimbursement from the Australian and French tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss for the applicable period. During the years ended December 31, 2017, 2016 and 2015, tax credits received were immaterial.

General and Administrative Expenses

General and administrative expenses include primarily personnel-related costs, stock-based compensation, professional fees for legal, consulting, audit and tax services, overhead expenses, such as rent, equipment depreciation, insurance and utilities, and other general operating expenses not otherwise included in research and development expenses. Our general and administrative expenses may increase in future periods if and to the extent we elect to increase our investment in infrastructure to support continued research and development activities and potential commercialization of our product candidates. We will continue to evaluate the need for such investment in conjunction with our ongoing consideration of our pipeline of product candidates. We anticipate increased expenses related to audit, legal and regulatory functions, as well as director and officer insurance premiums and investor relations costs associated with being a public reporting company.

Impairment of Goodwill and Intangible Assets

During the year ended December 31, 2016, due to a continuing decrease in our stock price that resulted in our market capitalization being less than the carrying value of our net assets and expected continuation of operating losses in subsequent years due to preclinical and expected clinical trials, we concluded that it was more likely than not that the fair value of our reporting unit was less than its carrying value. We performed a two-step goodwill impairment analysis and determined that our goodwill was fully impaired. As a result, we recorded a $49.5 million goodwill impairment charge in our consolidated statements of operations and comprehensive loss during the year ended December 31, 2016.

Additionally, in the fourth quarter of 2016, we performed our annual assessment for impairment of our intangible assets, ADVM-043 and ADVM-053. As a result of our decision to change our manufacturing process for ADVM-043 and ADVM-053 by implementing our proprietary baculovirus-based production system, we updated the related product development and manufacturing costs. We also reviewed and updated our expected timing of clinical trials, receipts of regulatory approvals and costs to complete for our ADVM-043 and ADVM-053 programs. Based upon our impairment analysis, we determined that the total carrying value of $16.2 million of our intangible assets was higher than their total fair value of $5.0 million. Accordingly, we recorded an $11.2 million impairment charge related to our intangible assets for the year ended December 31, 2016.

In the fourth quarter of 2017, we performed our annual impairment assessment of our intangible asset, ADVM-043, and concluded that our ADVM-043 intangible asset was not impaired.

As of December 31, 2017 and 2016, our intangible asset of $5.0 million was associated with ADVM-043. We are required to test our indefinite-lived intangible asset for impairment on an annual basis or more frequently if indicators of impairment exist. We operate as one reporting unit.

Other Income (Expense), Net

Other income (expense), net primarily comprises of interest income on our cash equivalents and investments in marketable securities.

Critical Accounting Policies, Significant Judgments and Use of Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

We have primarily generated revenue through the license and research and collaboration arrangements with our strategic partners for the development and commercialization of product candidates.

The terms of these types of agreements may include (i) licenses to our technology, (ii) research and development services, and (iii) services or obligations in connection with participation in research or steering committees. Payments to us under these arrangements typically include one or more of the following: nonrefundable upfront and license fees, research funding, milestone and other contingent payments for the achievement of defined collaboration objectives and certain preclinical, clinical, and regulatory events, as well as royalties on sales of any commercialized products.

In arrangements involving the delivery of more than one element, each required deliverable is evaluated to determine whether it qualifies as a separate unit of accounting. The determination is based on whether the deliverable has "standalone value" to the customer. If a deliverable does not qualify as a separate unit of accounting, it is combined with the other applicable undelivered item(s) within the arrangement and these combined deliverables are treated as a single unit of accounting.

The arrangement's consideration that is fixed or determinable is allocated to each separate unit of accounting based on the relative selling price methodology in accordance with the selling price hierarchy, which includes vendor-specific objective evidence ("VSOE") of selling price, if available, or third-party evidence of selling price if VSOE is not available, or the best estimate of selling price, if neither VSOE nor third-party evidence is available.

Payments or reimbursements for our research and development efforts for the arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis. When upfront payments are received and if there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, we recognize revenue ratably over the associated period of performance.

Our collaboration and license agreements may include contingent payments related to specified research, development and regulatory milestones. Such payments are typically payable under the collaborations when the collaboration partner claims or selects a target, or initiates or advances a covered product candidate in preclinical or clinical development, upon submission for marketing approval of a covered product with regulatory authorities, upon receipt of actual marketing approvals of a covered product or for additional indications, or upon the first commercial sale of a covered product. Each contingent and milestone payment is evaluated to determine whether it is substantive and at risk to both parties. We recognize any payment that is contingent upon the achievement of a substantive milestone entirely in the period in which the milestone is achieved. Any payments that are contingent upon achievement of a non-substantive milestone are recognized as revenue prospectively, when such payments become due and collectible, over the remaining expected performance period under the arrangement, which is generally the remaining period over which the research and development services are expected to be provided.

Accrued and Prepaid Research and Development Expense

We estimate our accrued and prepaid research and development expenses as of each balance sheet date. This process involves reviewing contracts and purchase orders, reviewing the terms of our license agreements, communicating with our applicable 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 actual cost. The majority of our service providers invoice us monthly in arrears for services performed. Expenses that are paid in advance of performance are deferred as a prepaid expense and expensed as the services are provided.

Examples of estimated accrued research and development expenses include fees to:

- contract manufacturers in connection with the production of clinical trial materials;
- CROs and other service providers in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors in connection with preclinical development activities; and
- services providers for professional service fees such as consulting and related services.

Our understanding of the status and timing of services performed relative to the actual status and timing may vary and may result in our reporting changes in estimates in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred. However, due to the nature of these estimates, we cannot assure you that we will not adjust our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies or other research activities. For the years ended December 31, 2017 and 2016, there were no material changes from our estimates of accrued research and development expenses.

Stock-Based Compensation Expense

We recognize compensation costs related to stock-based awards granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant-date fair value, and the resulting stock-based compensation expense, using the Black-Scholes valuation model for stock options, and using intrinsic value, which is the closing price of our common stock on the date of the grant for the restricted stock units, or RSUs. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. We use the Black-Scholes valuation model to assist us in determining the fair value of our stock options, which includes employee stock purchase plan. As of January 1, 2017, we adopted Accounting Standard Update ("ASU") No. 2016-09 and elected to account for forfeitures as they occur using a modified retrospective transition method, which requires us to record cumulative-effect adjustment to accumulated deficit. We determined that the impact of this adoption was immaterial, and no adjustments were recorded in our consolidated financial statements. Prior to the adoption of ASU No. 2016-09, stock-based compensation expense recognized for the portion of the award that is expected to vest was reduced by an estimated forfeiture rate. The Black-Scholes valuation model requires the use of following assumptions:

Expected volatility. We estimate expected volatility based on the average historical volatility of a peer group of comparable publicly traded life sciences and biotechnology companies with product candidates in similar stages of clinical development, as we do not have sufficient trading history for our common stock. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Expected term. We derived the expected term using the "simplified" method (the expected term is determined as the average of the time-to-vesting and the contractual life of the options), as we have limited historical information to develop expectations about future exercise patterns and post vesting employment termination behavior. Expected term for non-employee awards is based on the remaining contractual term of an option on each measurement date. The expected term of the Employee Stock Purchase Plan ("ESPP") rights equals to the six-month look-back period.

Risk-free interest rate. The risk-free interest rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term on the options.

Expected dividend yield. We have never paid any dividends and do not plan to pay dividends in the foreseeable future, and, therefore, used an expected dividend yield of zero in the valuation model.

Valuation of Long-Lived Assets and Purchased Intangible Asset

We evaluate the carrying value of amortizable long-lived assets, whenever events, or changes in business circumstances or the planned use of long-lived assets indicate that their carrying amounts may not be fully recoverable or that their useful lives are no longer appropriate. If these facts and circumstances exist, we assess for recovery by comparing the carrying values of long-lived assets with their future undiscounted net cash flows. If the comparison indicates that impairment exists, long-lived assets are written down to their respective fair value based on discounted cash flows. Significant management judgment is required in the forecast of future operating results that is used in the preparation of expected undiscounted cash flows. If management's assumptions about future operating results were to change as a result of events or circumstances, we may be required to record an impairment loss on these assets. No impairment indicators were noted for our amortizable long-lived assets, fixed assets, in the periods presented.

We also evaluate the carrying value of our intangible asset, not subject to amortization, related to in-process research and development ("IPR&D"), which is considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. Accordingly, amortization of the IPR&D asset will not occur until the product reaches commercialization. During the period the asset is considered indefinite-lived, it is tested for impairment on an annual basis, as well as between annual tests if we become aware of any events occurring or changes in circumstances that would indicate that the fair value of the IPR&D asset is less than its carrying amount. Impairment loss is recorded when fair value of an IPR&D asset is less than its carrying value. If the related project is terminated or abandoned, we will also have an impairment related to the IPR&D asset.

If and when development is complete, which generally occurs when regulatory approval to market the product is obtained, the associated IPR&D asset would be deemed definite-lived and would then be amortized based on its estimated useful life at that point in time based on respective patent term and tested for impairment only when impairment indicators are present as discussed above under long-lived assets.

Income Tax

On December 22, 2017, the U.S. government enacted comprehensive tax legislation, commonly known as the Tax Cuts and Jobs Act of 2017, or the Act, which significantly reforms the Internal Revenue Code of 1986, as amended. The Act contains broad and complex changes to corporate taxation, including in part reduction of the U.S. federal corporate tax rate from 35% to 21%, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously considered permanently reinvested, and creates new taxes on certain foreign sourced earnings.

As of December 31, 2017, we were able to determine a reasonable estimate, namely the one-time transition tax and the remeasurement of deferred tax at the new tax rate, we didn't recognize any provisional tax expense due to our significant operating losses.

The one-time transition tax is based on our post-1986 foreign earnings and profits which we had previously excluded from U.S. income taxes due to our position that we would permanently reinvest our future earnings. The one-time transition tax is applied at a 15.5% tax rate on cash assets and an 8% tax rate for other specified assets. Since our foreign operations incurred aggregated losses, we did not record provisional amount for our one-time transition tax liability for our foreign subsidiaries.

Additionally, the SEC staff has issued SAB 118, which allows us to record provisional amounts during a measurement period not to extend beyond one year of the enactment date. On December 22, 2017, Staff Accounting Bulletin No. 118 ("SAB 118") was issued to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Act. Because the Company is still in the process of analyzing certain provisions of the Act including the application of new executive compensation limitation provisions under Internal Revenue Section 162(m) in accordance with SAB 118, the Company determined that the adjustment to its deferred taxes was a provisional amount and a reasonable estimate at December 31, 2017.

We recognize deferred income taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. We periodically evaluate the positive and negative evidence bearing upon realizability of our deferred tax assets. Based upon the weight of available evidence, which includes our historical operating performance, reported cumulative net losses since inception and difficulty in accurately forecasting our future results, we maintained a full valuation allowance on the net deferred tax assets as of December 31, 2017 and 2016 of approximately $35.5 million and $23.4 million, respectively. We intend to maintain a full valuation allowance on the federal, state and foreign deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance.

As of December 31, 2017, we had U.S. federal net operating loss ("NOL") carryforwards of approximately $53.2 million to offset future federal income. NOLs expire at various years beginning with 2036. As of December 31, 2017, we also had U.S. state NOL carryforwards of approximately $37.8 million to offset future state income. U.S. State NOLs expire at various years beginning with 2036. At December 31, 2017, we also had approximately $44.1 million of foreign net operating loss carryforwards which may be available to offset future foreign income; these carryforwards do not expire.

Under Section 382 of the Code, our ability to utilize NOL carryforwards or other tax attributes such as research tax credits, in any taxable year may be limited if we have experienced an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who own at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. Due to a May 11, 2016 ownership change, we determined that certain NOLs for both federal and state purposes are severely limited and therefore we removed a significant amount NOL from our deferred tax assets.

We record unrecognized tax benefits as liabilities and adjust these liabilities when our judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from our current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. Our policy is to recognize interest and penalties related to income taxes as a component of income tax expense. No interest and penalties related to income taxes have been recognized in the consolidated statements of operations and comprehensive loss during the years ended December 31, 2017, 2016 and 2015.

Recent Accounting Standard Update— In May 2014, the Financial Accounting Standards Board ("FASB") issued ASU No. 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in ASC 605*, Revenue Recognition*. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 defines a five-step process to achieve this core principle and, in doing so, it is possible more judgment and estimates may be required within the revenue recognition process than required under existing U.S. GAAP including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 is required to be adopted, using either of two methods: (i) retrospective to each prior reporting period presented with the option to elect certain practical expedients as defined within ASU 2014-09; or (ii) retrospective with the cumulative effect of initially applying ASU 2014-09 recognized at the date of initial application and providing certain additional disclosures. In July 2015, the FASB voted to approve a one-year deferral of the effective date to December 15, 2017 for interim and annual reporting periods beginning after that date and permitted early adoption of the standard, but not before the original effective date of December 15, 2016. The FASB issued supplemental adoption guidance and clarification to ASU 2014-09 in March 2016, April 2016, May 2016, December 2016 and November 2017 within ASU 2016-08 *Revenue From Contracts With Customers: Principal vs. Agent Considerations*, ASU 2016-10 *Revenue From Contracts with Customers: Identifying Performance Obligations and Licensing*, ASU 2016-12 *Revenue from Contracts with Customers: Narrow-Scope Improvements and Practical Expedients,* ASU 2016-20 *Technical Corrections and Improvement to Topic 606 – Revenue from Contracts with Customers* and ASU 2017-14 *Reporting Comprehensive Income (Topic 220), Revenue Recognition (Topic 605), and Revenue from Contracts with Customers (Topic 606)*, respectively. We will adopt the new standard in the first quarter of 2018 using the retrospective approach noted in (ii) above. We concluded that our collaboration agreements with Regeneron and Editas will be impacted by the adoption of the new revenue standards. We are in the process of allocating the transaction price to the performance obligations in each of the contracts. Preliminarily, we anticipate a material impact to our accounting policies, business processes, internal controls and disclosures.

In January 2016, the FASB issued ASU No. 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities*, which amends the current guidance on the classification and measurement of financial instruments. Although this ASU retains many current requirements, it significantly revises an entity's accounting related to (i) the classification and measurement of investments in equity securities and (ii) the presentation of certain fair value changes for financial liabilities measured at fair value. This ASU also amends certain disclosure requirements associated with the fair value of financial instruments. The new standard is effective for fiscal years and interim periods within those fiscal years beginning after December 15, 2017, with early adoption permitted for certain changes. This ASU will be effective for us in the first quarter of 2018 and must be adopted using a modified retrospective approach, with certain exceptions. The adoption of this standard is not expected to have a significant impact on our consolidated financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-2, *Leases*, which amends the current guidance on leasing activities to provide more transparency and comparability and requires that all leases be recognized by lessees on their balance sheet as a right-of-use asset and corresponding lease liability, which are currently accounted for as operating leases. The new standard is effective for fiscal years and interim periods within those fiscal years beginning after December 15, 2018, with early adoption permitted. This ASU will be effective for us in the first quarter of 2019 and must be adopted using a modified retrospective transition approach. We have not yet determined whether we will elect early adoption and are currently evaluating the impact of the adoption of this standard on our consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU No. 2016-13 *Measurement of Credit Losses on Financial Instruments*. This ASU requires measurement and recognition of expected credit losses for financial assets held. The new standard is effective for fiscal years beginning after December 15, 2020 and interim periods beginning after December 15, 2021 with early adoption permitted beginning in the first quarter of 2019. This ASU will be effective for us in the first quarter of 2021 and must be adopted using a modified retrospective approach, with certain exceptions. We have not yet determined whether we will elect early adoption and are currently evaluating the impact of the adoption of this standard on our consolidated financial statements and related disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*, which clarifies the presentation and classification of certain cash receipts and cash payments in the statement of

cash flows. This ASU is effective for annual reporting periods beginning after December 15, 2017, and interim periods within that reporting period. Early adoption is permitted. This ASU will be effective for us in the first quarter of 2018. We are currently evaluating the impact of the adoption of this standard on our consolidated financial statements and related disclosures.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*, which provides amendments to current guidance to address the classification and presentation of changes in restricted cash in the statement of cash flows. This ASU is effective for annual reporting periods beginning after December 15, 2017, and interim periods within that reporting period. Early adoption is permitted. This ASU will be effective for us in the first quarter of 2018. We are currently evaluating the impact of the adoption of these standards on our consolidated financial statements and related disclosures.

In May 2017, the FASB issued ASU No. 2017-09, *Scope of Modification Accounting*, which provides amendments to the current guidance for modification accounting. This ASU clarifies that an entity should account for the effects of a modification unless all the following criteria are met: (1) the fair value of the modified award is the same as the fair value of the original award immediately before the original award is modified, (2) the vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified, and (3) the classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. This ASU is effective for annual reporting periods beginning after December 15, 2017, and interim periods within that reporting period. Early adoption is permitted. This ASU will be effective for us in the first quarter of 2018. We are currently evaluating the impact of the adoption of these standards on our consolidated financial statements and related disclosures.

Emerging Growth Company Status

We are an "emerging growth company" as defined in the JOBS Act, and therefore we may take advantage of certain exemptions from various public company reporting requirements. As an "emerging growth company,"

- we will avail ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act;
- we will provide less extensive disclosure about our executive compensation arrangements; and
- we will not require stockholder non-binding advisory votes on executive compensation or golden parachute arrangements.

However, we are choosing to irrevocably opt out of the extended transition periods available under the JOBS Act for complying with new or revised accounting standards. We will remain an "emerging growth company" for up to five years, although we will cease to be an "emerging growth company" upon the earliest of: (1) December 31, 2019; (2) the last day of the first fiscal year in which our annual gross revenues are $1.0 billion or more; (3) the date on which we have, during the previous rolling three-year period, issued more than $1.0 billion in non-convertible debt securities; and (4) the date on which we are deemed to be a "large accelerated filer" as defined in the Exchange Act.

Results of Operations

Our results of operations include the operations of Annapurna since May 11, 2016, the date of the Annapurna acquisition.

Comparison of the Years Ended December 31, 2017 and 2016

The following table summarizes our results of operations for the periods indicated:

	Years ended December 31,		
	2017	2016	Increase/(Decrease)
	(In thousands)		
Collaboration and license revenue	$ 1,849	$ 1,455	$ 394
Operating expenses:			
Research and development	39,839	31,670	8,169
General and administrative	20,857	24,355	(3,498)
Impairment of goodwill and intangible assets	—	60,714	(60,714)
Total operating expenses	60,696	116,739	(56,043)
Operating loss	(58,847)	(115,284)	56,437
Other income (expense), net	2,700	762	1,938
Net loss before income tax benefit	(56,147)	(114,522)	58,375
Income tax benefit	—	775	(775)
Net loss attributable to common stockholders	$ (56,147)	$ (113,747)	$ 57,600

Revenue

Collaboration and license revenue increased to $1.8 million for the year ended December 31, 2017 from $1.5 million for the year ended December 31, 2016. The increase was due to the recognition of additional deferred revenue related to billings for license and research services to Regeneron and Editas during the year ended December 31, 2016. During the year ended December 31, 2017, no additional deferred revenue or billings related to license and research services were recorded.

Research and Development Expense

Research and development expense increased to $39.8 million for the year ended December 31, 2017, from $31.7 million for the year ended December 31, 2016. The increase in research and development expense was primarily due to higher material production costs mainly for ADVM-043 for A1AT deficiency.

For the periods presented, our research and development activities are primarily for our A1AT deficiency, wAMD and HAE programs and earlier-stage research programs. We expect that research and development expenses will increase in future periods as we continue to invest in our three lead gene therapy programs and earlier-stage research programs.

General and Administrative Expense

General and administrative expense decreased to $20.9 million for the year ended December 31, 2017 from $24.4 million for the year ended December 31, 2016. The decrease in general and administrative expense was primarily due to $3.9 million of lower consulting and professional expenses, mainly attributable to the Annapurna acquisition activities and stockholders' litigation the during the year ended December 31, 2016, and $1.7 million of lower compensation expense mainly attributable to one-time charges of stock-based compensation expense related accelerated vesting of exiting executive employees' stock awards during the year ended December 31, 2016. This decrease was partially offset by $2.0 million of estimated termination costs associated with our master service agreement with Cornell University recorded during the year ended December 31, 2017.

We expect general and administrative expenses will increase in future periods to support continued research and development initiatives of our product candidates. We will continue to assess such expenses as we advance our three lead gene therapy programs and earlier-stage research programs.

Goodwill and Intangible Assets Impairment Charge

During the year ended December 31, 2016, we fully impaired our goodwill from the Annapurna acquisition and recorded a goodwill impairment charge of $49.5 million. Additionally, we recorded $11.2 million impairment charge related to our intangible assets for the year ended December 31, 2016. No impairment charges were recorded during the year ended December 31, 2017.

Other Income, Net

Other income, net increased to $2.7 million for the year ended December 31, 2017 from $0.8 million for the year ended December 31, 2016, primarily due to higher interest income as we increased our investments in marketable securities.

Income Tax Benefit

During the year ended December 31, 2016, we recorded income tax benefit of $0.8 million related to the change in the deferred tax liabilities balance due to intangible assets impairment recognized in the same years. During the year ended December 31, 2017, no income tax expense (benefit) was recorded due to overall operating loss.

Comparison of the Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for the periods indicated:

	Years ended December 31,		
	2016	2015	Increase/(Decrease)
	(In thousands)		
Collaboration and license revenue	$ 1,455	$ 2,319	$ (864)
Operating expenses:			
Research and development	31,670	25,462	6,208
General and administrative	24,355	22,107	2,248
Impairment of goodwill and intangible assets	60,714	—	60,714
Restructuring charges	—	2,573	(2,573)
Total operating expenses	116,739	50,142	66,597
Operating loss	(115,284)	(47,823)	(67,461)
Other income, net	762	370	392
Net loss before income tax benefit	(114,522)	(47,453)	(67,069)
Income tax benefit	775	—	775
Net loss attributable to common stockholders	$ (113,747)	$ (47,453)	$ (66,294)

Revenue

Collaboration and license revenue decreased to $1.5 million for the year ended December 31, 2016, from $2.3 million for the year ended December 31, 2015. The decrease of $0.9 million was primarily due to the recognition of $1.5 million related to the Regeneron time-limited right of first negotiation to license AVA-101 future development and commercialization in fiscal year 2015 offset by $0.6 million related to license and research services that are deferred and recognized over maximum research terms under the Regeneron and Editas agreements.

Research and Development Expense

Research and development expense increased to $31.7 million for the year ended December 31, 2016, from $25.5 million for the year ended December 31, 2015. The increase in research and development expense was primarily due to a $2.6 million increase in stock-based compensation expenses, including $0.9 million relating to the accelerated vesting of Annapurna options and shares recorded after the acquisition closing and $1.4 million related to the accelerated vesting of executive stock options and RSUs, $2.8 million increase for outside services expense related to the Cornell service agreement, $0.6 million increase in laboratory expense, $0.7 million increase in license fee expenses and $0.7 million increase in facilities allocation and depreciation charges, partially offset by $0.6 million decrease in materials expense, $0.4 million decrease in consulting and recruiting expenses, and $0.2 million decrease in compensation and benefits expenses.

General and Administrative Expense

General and administrative expense increased to $24.4 million for the year ended December 31, 2016, from $22.1 million for the year ended December 31, 2015. The increase in general and administrative expense was primarily due to increases of $2.5 million in Annapurna acquisition related expenses, $0.6 million increase in compensation and benefits, and $0.7 million in facilities allocation and depreciation expense, offset by $1.6 million decrease in stock-based compensation expense related to stock modifications for an executive officer's separation in 2015.

Impairment of Goodwill and Intangible Assets

We noted a continuing decrease in our stock price that resulted in our market capitalization being less than the carrying value of our net assets as of June 30, 2016 and the continuation of operating losses in subsequent years due to preclinical and expected clinical trials, we concluded that it is more likely than not that the fair value of our one reporting unit is less than its carrying value and concluded to perform a goodwill impairment analysis. We performed a two-step goodwill impairment analysis and recorded a $49.1 million and a $0.4 million goodwill impairment charge in the second and third quarter of 2016 in our consolidated statements of operations and comprehensive loss.

In the fourth quarter of 2016, we performed our annual assessment of our IPR&D assets. Based on our decision to change our manufacturing process for ADVM-043 and ADVM-053 by implementing our proprietary baculovirus-based production system, we updated the related manufacturing costs. As a result, we revised our forecasts for the manufacturing and related costs. In addition, we also reviewed and updated our expected timing of clinical trials, receipts of regulatory approvals, and costs to complete. Based upon our analysis, we determined that the carrying value of $16.2 million for our ADVM-043 and ADVM-053 IPR&D assets was higher than their fair value of $5.0 million. Accordingly, we recorded an $11.2 million IPR&D impairment charge for the year ended December 31, 2016.

Restructuring Charges

In connection with the restructuring of our workforce in the fourth quarter of 2015, we incurred aggregate restructuring charges of approximately $2.6 million related to one-time termination severance payments and other employee-related benefits, including approximately $1.0 million of stock-based compensation expense related to the acceleration of restricted stock units.

Other Income, Net

Other income, net is comprised primarily of interest income on our cash equivalents and investments in marketable securities for the years ended December 31, 2016 and 2015.

Income Tax Benefit

During the fourth quarter of 2016, we recorded income tax benefit of $0.8 million related to the change in the deferred tax liabilities balance due to intangible assets impairment recognized in the same quarter. During the year ended December 31, 2015, no income tax expense (benefit) was recorded due to overall operating loss.

Liquidity, Capital Resources and Plan of Operations

We have not generated positive cash flow or net income from operations since our inception and as of December 31, 2017, we had an accumulated deficit of $254.1 million. As of December 31, 2017, we had $190.5 million in cash, cash equivalents and short-term investments. We believe that our existing cash and cash equivalents as of December 31, 2017, together with the net proceeds the sales of our common stock pursuant to the 2017 stock offering agreement and from our February 2018 underwritten public offering of our common stock, will be sufficient to fund our operations through the end of 2019.

In August 2017, we entered into the 2017 stock offering agreement. Under the terms and conditions of the 2017 stock offering agreement, we may offer to sell our common stock for an aggregate offering price of up to $50.0 million through the agent from time to time. In January 2018, we sold a total of 1,419,893 shares of our common stock at market prices under the 2017 stock offering agreement and raised total net proceeds of $5.7 million, net of issuance costs. We have sold a total of 6,550,232 million shares of our common stock at market prices pursuant to the 2017 stock offering agreement and raised total net proceeds of approximately $22.5 million, net of issuance costs.

In February 2018, we completed an underwritten public offering for the sale of 10,222,235 shares of our common stock and raised total net proceeds of approximately $64.3 million, after discounts and other issuance costs.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates and ongoing internal research and development programs. At this time, we cannot reasonably estimate the nature, timing or aggregate amount of such costs. However, in order to complete our planned preclinical trials and current and future clinical trials, and to complete the process of obtaining regulatory approval for our product candidates, as well as to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding in the future.

If and when we seek additional funding, we will do so through equity or debt financings, collaborative or other arrangements with corporate sources or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital in the future could have a negative impact on our financial condition and our ability to pursue our business strategies. In order to complete development and commercialization of any of our product candidates, we anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the initiation, progress, timing, costs and results of preclinical studies and any clinical trials for our product candidates;
- the outcome, timing of and costs involved in, seeking and obtaining approvals from the Food and Drug Administration (FDA) and other regulatory authorities, including the potential for the FDA and other regulatory authorities to require that we perform more studies than those that we currently expect;
- the ability of our product candidates to progress through clinical development activities successfully;
- our need to expand our research and development activities;
- the rate of progress and cost of our commercialization of our products;
- the cost of preparing to manufacture our products on a larger scale;
- the costs of commercialization activities including product sales, marketing, manufacturing and distribution;
- the degree and rate of market acceptance of any products launched by us or future partners;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need to implement additional infrastructure and internal systems;
- our ability to hire additional personnel;
- our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements, and;
- the emergence of competing technologies or other adverse market developments.

If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license other technologies or clinical product candidates or programs that we would prefer to develop and commercialize ourselves.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods presented below:

	Years ended December 31,		
	2017	2016	2015
	(In thousands)		
Net cash (used in) provided by:			
Operating activities	$ (45,421)	$ (38,366)	$ (35,338)
Investing activities	(122,204)	38,775	(41,569)
Financing activities	16,748	556	138,860
Effect of changes in foreign currency exchange rates on cash and cash equivalents	(774)	(143)	(9)
Net (decrease) increase in cash and cash equivalents	$ (151,651)	$ 822	$ 61,944

Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2017, was $45.4 million, primarily as a result of the net loss of $56.1 million, mainly driven by our continued research and development activities, and $0.8 million of net decrease in operating assets and liabilities, partially offset by $11.5 million for non-cash charges.

Net cash used in operating activities for the year ended December 31, 2016, was $38.4 million, primarily as a result of the net loss of $113.7 million, partially offset by $60.7 million for non-cash charge related to goodwill and IPR&D assets impairment, $11.4 million for non-cash charge related to stock-based compensation expense, $1.6 million for depreciation and amortization expense and $1.6 million for net increase in operating assets and liabilities.

Net cash used in operating activities for the year ended December 31, 2015, was $35.3 million, primarily as a result of the net loss of $47.5 million, partially offset by $11.5 million for non-cash charge related to stock-based compensation, a $0.2 million non-cash stock compensation charge related to the issuance of warrant, $0.8 million for depreciation and amortization expense, $0.8 million for amortization of premium on marketable securities and $1.2 million for net decrease in operating assets and liabilities.

Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was $122.2 million for the year ended December 31, 2017, which consisted of the purchases of marketable securities of $209.8 million and purchases of property and equipment of $1.0 million, partially offset by $87.6 million maturities of marketable securities and $1.0 million sales of marketable securities.

Net cash provided by investing activities was $38.8 million for the year ended December 31, 2016, which consisted of the maturities of marketable securities of $37.7 million and $3.4 million cash acquired through our Annapurna acquisition, partially offset by purchases of property and equipment of $2.4 million.

Net cash used in investing activities was $41.6 million for the year ended December 31, 2015, which consisted of the purchases of marketable securities of $88.4 million, partially offset by maturities of marketable securities of $49.9 million and purchases of property and equipment of $3.0 million.

Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2017, of $16.7 million, which consisted of $16.5 million of net proceeds from the sales of our common stock under the 2017 stock offering agreement, net of issuance costs, $0.5 million from proceeds from the exercise of stock options and purchases of common stock under employee stock purchase plan, partially offset by $0.3 million in taxes paid relating to net share settlement of restricted stock units.

Net cash provided by financing activities for the year ended December 31, 2016, of $0.6 million, which consisted of $0.9 million from proceeds relating to the exercise of options for common shares and employee stock purchase plan purchases and $0.1 million relating to funds received from a financing arrangement, partially offset by $0.5 million in taxes paid relating to net share settlement of restricted stock units.

Net cash provided by financing activities for the year ended December 31, 2015, of $138.9 million, which consisted of $130.6 million net proceeds from our follow-on offering in January 2015 and $8.3 million from sale of common shares.

Contractual Obligations and Commitments

We have lease obligations consisting of an operating lease for our operating facility that expires in 2020. Additionally, we have contractual obligations to vendors.

The following table summarizes our contractual obligations as of December 31, 2017:

	Payment Due by Period		
	Less Than 1 Year	1 to 3 Years	Total
	(In thousands)		
Operating lease obligations	$ 1,162	$ 1,600	$ 2,762
Master service agreement with Cornell (1)	2,000	—	2,000
BPI financing	120	397	517
Contractual obligations (2)	4,187	—	4,187
Total	$ 7,469	$ 1,997	$ 9,466

(1) Costs associated with the termination of the master service agreement with Cornell recorded within accrued expenses and other current liabilities in our consolidated balance sheet as of December 31, 2017 and within general and administrative expenses in our consolidated statement of operations and comprehensive loss for the year ended December 31, 2017.

(2) Related to our contract manufacturing with a vendor for materials production for our three programs, ADVM-022, ADVM-043 and ADVM-053.

The lease agreement provides for an escalation of rent payments each year and will expire on May 8, 2020. We may extend the lease term for up to four years. As of December 31, 2017, we had various open purchase orders with various vendors for our research and development and general and administrative activities.

We have received $0.2 million funding from The Alpha-1 Project, Inc. (the "TAP financing") for a sponsored research agreement entered into in July 2016. The TAP financing was recorded within other non-current liabilities in our balance sheets. We may pay up to 4.5 times of the received amount if and when certain product approval and sales milestones are achieved.

We are obligated to make future payments to third parties under in-license agreements, including sublicense fees, royalties and payments that become due and payable on the achievement of certain development and commercialization milestones. As the amount and timing of sublicense fees and the achievement and timing of these milestones are not probable and estimable, such commitments have not been included on our balance sheet or in the contractual obligations tables above.

Off Balance Sheet Arrangements

We do not have any off-balance sheet arrangements as defined in Regulation S-K, Item 303(a)(4)(ii).

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Foreign Currency Exchange Risk

A portion of our operating expenses are incurred outside the U.S. and are denominated in foreign currencies and are subject to fluctuations due to changes in foreign currency exchange rates, particularly changes in the Euro and Australian dollar. Additionally, fluctuations in foreign currency exchange rates may cause us to recognize transaction gains and losses in our statement of operations. To date, foreign currency transaction gains and losses have not been material to our consolidated financial statements, and we have not engaged in any foreign currency hedging transactions. As our international operations grow, we will continue to reassess our approach to managing the risks relating to fluctuations in currency rates.

Interest Rate Risk

We had cash and cash equivalents and short-term investments of $190.5 million as of December 31, 2017, consisting of cash, money market funds, government securities, commercial paper, certificates of deposit and corporate bond, and cash and cash equivalents of $222.2 million as of December 31, 2016, consisting of cash and money market funds. To date, fluctuations in interest income have not been significant.

We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed to, nor do we anticipate being exposed to, material risks due to changes in interest rates. A hypothetical 10% change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data.

ADVERUM BIOTECHNOLOGIES, INC.
CONSOLIDATED FINANCIAL STATEMENTS
AS OF DECEMBER 31, 2017AND 2016
AND FOR THE YEARS ENDED DECEMBER 31, 2017, 2016 AND 2015

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Adverum Biotechnologies, Inc.
Menlo Park, California

Opinion on the Financial Statements

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

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/ Deloitte & Touche LLP

San Jose, California
March 6, 2018

We have served as the Company's auditor since 2013.

ADVERUM BIOTECHNOLOGIES, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	As of December 31,	
	2017	**2016**
Assets		
Current assets:		
Cash and cash equivalents	$ 70,519	$ 222,170
Short-term investments	119,966	—
Receivable from collaborative partner	—	886
Prepaid expenses and other current assets	3,256	2,218
Total current assets	193,741	225,274
Property and equipment, net	3,024	4,169
Deposit and other non-current assets	140	140
Intangible asset	5,000	5,000
Total assets	$ 201,905	$ 234,583
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,731	$ 1,474
Accrued expenses and other current liabilities	6,964	6,476
Deferred rent, current portion	129	96
Deferred revenue, current portion	1,850	1,850
Total current liabilities	10,674	9,896
Long-term liabilities:		
Deferred rent, net of current portion	222	352
Deferred revenue, net of current portion	5,250	7,099
Deferred tax liability, non-current	1,250	1,250
Other non-current liabilities	481	386
Total liabilities	17,877	18,983
Commitments and contingencies (Note 11)		
Stockholders' equity:		
Preferred stock, $0.0001 par value, 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.0001 par value, 300,000,000 shares authorized at December 31, 2017 and 2016; 49,015,339 and 41,805,009 shares issued and outstanding at December 31, 2017 and 2016, respectively	5	4
Additional paid-in capital	439,048	413,518
Accumulated other comprehensive loss	(963)	(7)
Accumulated deficit	(254,062)	(197,915)
Total stockholders' equity	184,028	215,600
Total liabilities and stockholders' equity	$ 201,905	$ 234,583

See accompanying notes to consolidated financial statements.

ADVERUM BIOTECHNOLOGIES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except per share data)

	Years ended December 31,		
	2017	2016	2015
Collaboration and license revenue	$ 1,849	$ 1,455	$ 2,319
Operating expenses:			
Research and development	39,839	31,670	25,462
General and administrative	20,857	24,355	22,107
Impairment of goodwill and intangible assets	—	60,714	—
Restructuring charges	—	—	2,573
Total operating expenses	60,696	116,739	50,142
Operating loss	(58,847)	(115,284)	(47,823)
Other income:			
Other income, net	2,700	762	370
Total other income, net	2,700	762	370
Net loss before income taxes	(56,147)	(114,522)	(47,453)
Income tax benefit	—	775	—
Net loss attributable to common stockholders	$ (56,147)	$ (113,747)	$ (47,453)
Other comprehensive loss:			
Net unrealized gain (loss) on marketable securities	(182)	6	(6)
Foreign currency translation adjustment	(774)	(2)	(15)
Comprehensive loss	$ (57,103)	$ (113,743)	$ (47,474)
Net loss per share attributable to common stockholders-basic and diluted	$ (1.29)	$ (3.14)	$ (1.86)
Weighted-average common shares outstanding-basic and diluted	43,661	36,246	25,479

See accompanying notes to consolidated financial statements.

ADVERUM BIOTECHNOLOGIES, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands except share and per share data)

	COMMON STOCK $0.0001 PAR VALUE		ADDITIONAL PAID-IN	ACCUMULATED OTHER COMPREHENSIVE	ACCUMULATED	TOTAL STOCKHOLDERS'
	Shares	Amount	CAPITAL	INCOME (LOSS)	DEFICIT	EQUITY
Balance at December 31, 2014	**22,754,037**	**$ 2**	**$ 186,186**	**$ 10**	**$ (36,715)**	**$ 149,483**
Issuance of common stock, net of issuance costs of $11,099	2,599,375	1	138,953	—	—	138,954
Issuance of common stock warrants in consideration for services	—	—	218	—	—	218
Stock-based compensation expense	—	—	11,505	—	—	11,505
Common stock issued upon exercise of stock options	399,434	—	188	—	—	188
Common stock issued under employee stock purchase plan	19,577	—	145	—	—	145
Common stock issued upon release of restricted stock units	132,397	—	—	—	—	—
Restricted stock surrendered for taxes	(46,098)	—	(427)	—	—	(427)
Net unrealized loss on marketable securities	—	—	—	(6)	—	(6)
Foreign currency translation adjustments	—	—	—	(15)	—	(15)
Net loss	—	—	—	—	(47,453)	(47,453)
Balance at December 31, 2015	**25,858,722**	**3**	**336,768**	**(11)**	**(84,168)**	**252,592**
Issuance of common stock in consideration of acquisition	14,087,246	1	64,844	—	—	64,845
Remeasurement of contingent common stock warrant in consideration for services	—	—	8	—	—	8
Issuance of warrant in connection with financing arrangement	—	—	26	—	—	26
Stock-based compensation expense	—	—	11,416	—	—	11,416
Common stock issued upon exercise of stock options	1,525,687	—	763	—	—	763
Common stock issued under employee stock purchase plan	56,696	—	186	—	—	186
Common stock issued upon release of restricted stock units	385,524	—	—	—	—	—
Restricted stock surrendered for taxes	(108,866)	—	(493)	—	—	(493)
Net unrealized gain on marketable securities	—	—	—	6	—	6
Foreign currency translation adjustments	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	(113,747)	(113,747)
Balance at December 31, 2016	**41,805,009**	**4**	**413,518**	**(7)**	**(197,915)**	**215,600**
Issuance of common stock, net of issuance costs of $230	5,130,339	1	16,518	—	—	16,519
Remeasurement of contingent common stock warrant in consideration for services	—	—	60	—	—	60
Stock-based compensation expense	—	—	8,723	—	—	8,723
Common stock issued upon exercise of stock options	1,808,696	—	367	—	—	367
Common stock issued under employee stock purchase plan	74,642	—	175	—	—	175
Common stock issued upon release of restricted stock units	307,610	—	—	—	—	—
Restricted stock surrendered for taxes	(110,957)	—	(313)	—	—	(313)
Net unrealized loss on marketable securities	—	—	—	(182)	—	(182)
Foreign currency translation adjustments	—	—	—	(774)	—	(774)
Net loss	—	—	—	—	(56,147)	(56,147)
Balance at December 31, 2017	**49,015,339**	**$ 5**	**$ 439,048**	**$ (963)**	**$ (254,062)**	**$ 184,028**

See accompanying notes to consolidated financial statements.

ADVERUM BIOTECHNOLOGIES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Years ended December 31,		
	2017	**2016**	**2015**
Cash flows from operating activities:			
Net loss	$ (56,147)	$ (113,747)	$ (47,453)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	2,096	1,603	812
Stock-based compensation expense	8,723	11,416	11,505
Amortization of premium on marketable securities	593	—	780
Impairment of goodwill and intangible assets	—	60,714	—
Non-cash research and development expense	60	8	218
Other	10	—	21
Changes in operating assets and liabilities:			
Accounts receivable, net	886	(437)	(6)
Prepaid expenses and other current assets	(491)	71	(531)
Deposit and other long-term assets	—	—	(3)
Accounts payable	333	(111)	(312)
Accrued expenses and other current liabilities	487	(190)	724
Restructuring liabilities	(25)	(988)	1,013
Deferred revenue	(1,849)	3,360	(2,313)
Deferred rent	(97)	(65)	207
Net cash used in operating activities	(45,421)	(38,366)	(35,338)
Cash flows from investing activities:			
Purchases of marketable securities	(209,787)	—	(88,427)
Sales of marketable securities	1,003	—	—
Maturities of marketable securities	87,596	37,738	49,850
Purchases of property and equipment	(1,016)	(2,412)	(2,992)
Cash acquired in business acquisition	—	3,449	—
Net cash (used in) provided by investing activities	(122,204)	38,775	(41,569)
Cash flows from financing activities:			
Proceeds from offering of common stock, net of issuance costs	16,519	—	138,954
Proceeds from issuance of common stock pursuant to option exercises	367	763	188
Taxes paid related to net share settlement of restricted stock units	(313)	(493)	(427)
Proceeds from employee stock purchase plan	175	186	145
Proceeds from a financing arrangement	—	100	—
Net cash provided by financing activities	16,748	556	138,860
Effect of foreign currency exchange rate on cash and cash equivalents	(774)	(143)	(9)
Net (decrease) increase in cash and cash equivalents	(151,651)	822	61,944
Cash and cash equivalents at beginning of period	222,170	221,348	159,404
Cash and cash equivalents at end of period	$ 70,519	$ 222,170	$ 221,348
Supplemental schedule of noncash investing and financing information			
Issuance of common stock and exchange of stock options for business acquisition	$ —	$ 64,845	$ —
Fixed assets in accounts payable and current liabilities	$ 115	$ 180	$ 178

See accompanying notes to consolidated financial statements.

1. Description of the business

Nature of Business—Adverum Biotechnologies, Inc. (the "Company" or "Adverum") was incorporated in Delaware on July 17, 2006 as Avalanche Biotechnologies, Inc. and changed its name to Adverum Biotechnologies, Inc. on May 11, 2016. The Company is headquartered in Menlo Park, California. The Company is a clinical-stage gene therapy company targeting unmet medical needs in serious rare and ocular diseases. Leveraging a next-generation adeno-associated virus ("AAV")-based directed evolution platform, the Company generates gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. The Company's core capabilities include clinical development and in-house manufacturing expertise, specifically in process development, assay development, and current Good Manufacturing Practices ("cGMP") quality control. Adverum is advancing a robust pipeline of gene therapy product candidates designed to treat rare diseases alpha-1 antitrypsin ("A1AT") deficiency and hereditary angioedema ("HAE"), as well as wet age-related macular degeneration ("wAMD"). Since the Company's inception, it has devoted its efforts principally to performing research and development activities, including conducting preclinical studies, early clinical trials, filing patent applications, obtaining regulatory agreements, hiring personnel, and raising capital to support these activities.

The Company has not generated any revenue from the sale of products since its inception. The Company has experienced net losses since its inception and had an accumulated deficit of $254.1 million as of December 31, 2017. The Company expects to incur losses and have negative net cash flows from operating activities as it engages in further research and development activities. The Company believes that it has sufficient funds to continue operations through the end of 2019.

In May 2016, the Company completed the acquisition of all the outstanding shares of Annapurna Therapeutics SAS ("Annapurna"), a privately-held French gene therapy company, in accordance with the terms of the acquisition agreement (the "Annapurna acquisition") dated as of January 29, 2016, as amended on April 6, 2016. As a result, Annapurna is now a wholly owned subsidiary of the Company. Refer to Note 3 for more details.

Upon completion of the Annapurna acquisition, the Company changed its name to "Adverum Biotechnologies, Inc." The Company's shares of common stock listed on The Nasdaq Global Market, previously trading through the close of business on Wednesday, May 11, 2016 under the ticker symbol "AAVL," commenced trading on The Nasdaq Global Market under the ticker symbol "ADVM" on Thursday, May 12, 2016.

Initial Public and Follow-on Offerings—In August 2014 and January 2015, the Company completed its initial public offering (IPO) and concurrent private placement and a follow-on offering and raised a total of net proceeds of $237.1 million. In March 2015, (i) the Company received net proceeds of approximately $8.3 million, after discounts and other issuance costs, which resulted from the sale of 230,000 shares of its common stock, and (ii) the Company issued 230,000 shares of its common stock to a stockholder that exercised warrants prior to the IPO.

In August 2017, the Company entered into an at-the-market sales agreement with an agent for the sales of its common stock at market price (the "2017 stock offering agreement"). Under the terms and conditions of the 2017 stock offering agreement, the Company may offer to sell its common stock for an aggregate offering price of up to $50.0 million through the agent from time to time. During the year ended December 31, 2017, the Company issued and sold a total of 5,130,339 shares of its common stock at market prices under the 2017 stock offering agreement and raised total net proceeds of $16.5 million, net of issuance costs. In January 2018, the Company issued and sold a total of 1,419,893 shares of its common stock at market prices under the 2017 stock offering agreement and raised total net proceeds of approximately $5.7 million, net of issuance costs (see Note 17).

In February 2018, the Company completed an underwritten public offering for the sale of 10,222,235 shares of its common stock and raised total net proceeds of approximately $64.3 million, after discounts and other issuance costs (see Note 17).

2. Summary of significant accounting policies

Basis of Presentation and Principles of Consolidation— The Company's consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP") and pursuant to the rules and regulations of the Securities and Exchange Commission ("SEC"). The consolidated financial statements include the accounts of the Company and its wholly-owned subsidiaries. All inter-company transactions and balances have been eliminated in consolidation.

Use of Estimates—The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of income and expenses during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. On an ongoing basis, the Company evaluates its estimates and assumptions, including those related to research and development expense accruals, stock-based compensation expense, income taxes, intangible asset, fair values of financial instruments and fair value of common stock warrants. The Company's actual results may differ from these estimates under different assumptions or conditions. There have been no significant changes from the Company's original estimates in any periods presented.

Foreign Currency Translation—The Company's consolidated financial statements are prepared in U.S. dollars. The Company's foreign subsidiaries use the Euro and Australian dollar as their functional currencies and maintain their records in their local currencies, except its Ireland subsidiary that uses the U.S. dollar as its functional currency. Assets and liabilities are re-measured at exchange rates in effect at the end of the reporting period for the Company's French and Australian subsidiaries, and at historical exchange rates for its Irish subsidiary. Equity is measured at historical rates and income and expenses are re-measured at average exchange rates for the reporting period. The resulting foreign currency translation adjustment is recorded in accumulated other comprehensive loss in the consolidated balance sheet. Transactions denominated in foreign currency are translated at exchange rates at the date of transaction with foreign currency gains (losses) recorded in other income (expense), net in the consolidated statements of operations and comprehensive loss.

Cash and Cash Equivalents—The Company considers all highly liquid investments purchased with original maturities of three months or less at the date of purchase to be cash equivalents. Cash and cash equivalents include cash held in banks, money market accounts and highly liquid debt securities. Cash equivalents are stated at fair value.

Short-Term Investments—All short-term investments, which consist of debt securities and certificates of deposit, have been classified as "available for sale" and are carried at fair value. Unrealized gains and losses, net of any related tax effects, are excluded from earnings and are included in other comprehensive loss and reported as a separate component of stockholders' equity until realized. Realized gains and losses and declines in value judged to be other than temporary, if any, on available-for-sale securities are included in other income (expense), net in the Company's consolidated statements of operations and comprehensive loss. The cost of securities sold is based on the specific-identification method. The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Interest on short-term investments is included in other income, net in the Company's consolidated statements of operations and comprehensive loss. In accordance with the Company's investment policy, management invests to diversify credit risk and only invests in securities with high credit quality, including U.S. government securities.

The Company periodically evaluates whether declines in the fair value of its investments below their cost are other than temporary. The evaluation includes consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities, and whether it is more likely than not that the Company will be required to sell the securities before the recovery of their amortized cost basis. If the Company determines that the decline in fair value of an investment is below its accounting basis and this decline is other than temporary, the Company would reduce the carrying value of the security it holds and records a loss for the amount of such decline. The Company has not recorded any realized losses or declines in value judged to be other than temporary on its investments.

Segment Reporting—The Company operates and manages its business as one reporting and operating segment, which is the business of developing and commercializing gene therapeutics. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance.

Concentrations of Credit Risk and Other Uncertainties—Financial instruments that potentially subject the Company to significant concentrations of credit risk consists primarily of cash, cash equivalents and short-term investments. Risks associated with cash, cash equivalents, short-term investments are mitigated by the Company's investment policy, which limits the Company's investing to only those marketable securities rated at least A-1/P-1 Short Term Rating and A/A2 Long Term Rating, as determined by independent credit rating agencies. Management believes that the Company is not exposed to significant credit risk.

The Company is subject to certain risks and uncertainties, including, but not limited to changes in any of the following areas that the Company believes could have a material adverse effect on future financial position or results of operations: ability to obtain future financing; regulatory approval and market acceptance of, and reimbursement for, the Company's product candidates; performance of third-party clinical research organizations and manufacturers; development of sales channels; protection of the intellectual property; litigation or claims against the Company based on intellectual property, patent, product, regulatory or other factors; and the Company's ability to attract and retain employees necessary to support the growth.

Property and Equipment—Property and equipment are recorded at cost, net of accumulated depreciation and amortization. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are capitalized and amortized over the shorter period of their expected lives or the lease term. Major replacements and improvements are capitalized, while general repairs and maintenance are expensed as incurred.

Valuation of Long-Lived Assets and Purchased Intangible Assets—The Company evaluates the carrying value of amortizable long-lived assets, whenever events, or changes in business circumstances or the planned use of long-lived assets indicate that their carrying amounts may not be fully recoverable or that their useful lives are no longer appropriate. If these facts and circumstances exist, the Company assesses for recovery by comparing the carrying values of long-lived assets with their future undiscounted net cash flows. If the comparison indicates that impairment exists, long-lived assets are written down to their respective fair values based on discounted cash flows. Significant management judgment is required in the forecasting of future operating results that is used in the preparation of expected undiscounted cash flows. If management's assumptions about future operating results were to change as a result of events or circumstances, the Company may be required to record an impairment loss on these assets. No impairment indicators were noted for the Company's amortizable long-lived assets, fixed assets, in the periods presented.

The Company also evaluates the carrying value of intangible asset (not subject to amortization) related to in-process research and development ("IPR&D") asset, which is considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. Accordingly, amortization of the IPR&D assets will not occur until the product reaches commercialization. During the period the intangible asset is considered indefinite-lived, it will be tested for impairment on an annual basis, as well as between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate that the fair value of the IPR&D asset is less than its carrying amount. If and when development is complete, which generally occurs when regulatory approval to market the product is obtained, the associated IPR&D asset would be deemed definite-lived and would then be amortized based on its estimated useful life at that point in time based on respective patent term. If a potential impairment exists, an impairment loss is measured as the excess of the asset's carrying value over its fair value. During the year ended December 31, 2016, the Company recorded an impairment charge of $11.2 million related to its intangible assets (see Note 3).

Financial Liabilities— During the year ended December 31, 2016, the Company entered into a sponsored research agreement with The Alpha-1 Project, Inc. (the "TAP") with an embedded derivative, the Company determined to account for this financial liability at fair value and recorded as other non-current liabilities in its consolidated balance sheets (see Note 6). Change in fair value is recorded within other income, net in the Company's consolidated statement of operations and comprehensive loss.

Revenue Recognition—The Company has primarily generated revenue through license, research and collaboration arrangements with its strategic partners.

The terms of these types of agreements may include (i) licenses to Adverum technology, (ii) research and development services, and (iii) services or obligations in connection with participation in research or steering committees. Payments to the Company under these arrangements typically include one or more of the following: nonrefundable upfront and license fees, research funding, milestone and other contingent payments for the achievement of defined collaboration objectives and certain preclinical, clinical, and regulatory events, as well as royalties on sales of any commercialized products.

In arrangements involving the delivery of more than one element, each required deliverable is evaluated to determine whether it qualifies as a separate unit of accounting. The determination is based on whether the deliverable has "standalone value" to the customer. If a deliverable does not qualify as a separate unit of accounting, it is combined with the other applicable undelivered item(s) within the arrangement and these combined deliverables are treated as a single unit of accounting.

The arrangement's consideration that is fixed or determinable is allocated to each separate unit of accounting based on the relative selling price methodology in accordance with the selling price hierarchy, which includes vendor-specific objective evidence ("VSOE") of selling price, if available, or third-party evidence of selling price if VSOE is not available, or the best estimate of selling price, if neither VSOE nor third-party evidence is available.

Payments or reimbursements for the Company's research and development efforts for the arrangements where such efforts are considered as deliverables are recognized as the services are performed and are presented on a gross basis. When upfront payments are received and if there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, the Company recognizes revenue ratably over the associated period of performance.

The Company's collaboration and license agreements may include contingent payments related to specified research, development and regulatory milestones. Such payments are typically payable under the collaborations when the collaboration partner claims or selects a target, or initiates or advances a covered product candidate in preclinical or clinical development, upon submission for

marketing approval of a covered product with regulatory authorities, upon receipt of actual marketing approvals of a covered product or for additional indications, or upon the first commercial sale of a covered product. Each contingent and milestone payment is evaluated to determine whether it is substantive and at risk to both parties. The Company recognizes any payment that is contingent upon the achievement of a substantive milestone entirely in the period in which the milestone is achieved. Any payments that are contingent upon achievement of a non-substantive milestone are recognized as revenue prospectively, when such payments become due and collectible, over the remaining expected performance period under the arrangement, which is generally the remaining period over which the research and development services are expected to be provided.

Collaboration and License Revenue

Editas Agreement—In August 2016, the Company entered into a collaboration, option and license agreement with Editas Medicine, Inc. ("Editas") (see Note 7). Under the terms of the agreement, the Company received initial payments of $1.0 million that included $0.5 million for research services during the year ended December 31, 2016. As the agreement provides for multiple deliverables, the Company accounts for this agreement as a multiple elements revenue arrangement. At the inception of the agreement, identified deliverables include research services, manufacturing of viral vectors for research, participation in joint research committee and exclusivity during the option period. These deliverables did not appear to have a standalone value and were combined into one unit of accounting. Options for each indication to license the Company's AAV vector are considered substantive options and do not include significant incremental discounts. Therefore, they are not considered as deliverables under the agreement. In January 2018, the Company and Editas extended the research collaboration, option and license agreement (see Note 7). In consideration for extending the agreement, Editas made a one-time payment, non-refundable cash payment of $0.5 million to the Company in February 2018.

The Company allocated the $1.0 million received to a single unit of accounting identified in the arrangement. The Company expects to recognize $1.0 million ratably over the associated period of performance, which is the maximum research period of three years. As there is no discernible pattern of performance and/or objectively measurable performance measures do not exist, the Company recognizes revenue on a straight-line basis. During the years ended December 31, 2017 and 2016, the Company recognized $0.3 million and $0.1 million, respectively, as collaboration and license revenue related to Editas agreement.

Regeneron Agreement—In May 2014, the Company entered into a research collaboration and license agreement with Regeneron Pharmaceuticals, Inc. ("Regeneron") to discover, develop and commercialize novel gene therapy products for the treatment of ophthalmologic diseases (see Note 7). Under the terms of the agreement, during the year ended December 31, 2014, the Company received initial upfront non-refundable cash payments of $8.0 million that included payment for research license fees, prepaid collaboration research costs and the time-limited right of first negotiation for license to develop and commercialize AVA-101. As the agreement provides for multiple deliverables, the Company accounts for this agreement as a multiple elements revenue arrangement. If deliverables did not appear to have a standalone value, they were combined with other deliverables into a unit of accounting with a standalone value. The Company allocated the $8.0 million to the relative fair value of the two units of accounting identified in the arrangement. The Company recognizes $6.5 million allocated to the first unit of accounting for the research licenses and related research and development services ratably over the associated period of performance, which is the maximum research period of eight years. As there was no discernible pattern of performance and/or objectively measurable performance measures did not exist for the first unit of accounting, the Company recognizes revenue on a straight-line basis over the eight years performance period. The remaining $1.5 million allocated to the second unit of accounting for the time-limited right of first negotiation for license to develop and commercialize AVA-101 was deferred. On November 2, 2015, Regeneron notified the Company that it did not exercise this right of first negotiation and the Company recognized the entire $1.5 million as revenue during the year ended December 31, 2015.

As original research budget was fully used in the fourth quarter of 2015, the Company and Regeneron will agree on the reimbursement of additional research expenses annually. The Company invoices for services performed quarterly. These additional research fees are added to the research licenses and related research and development services unit of accounting, recorded as deferred revenue and recognized to revenue over the remaining research term. During the years ended December 31, 2017, 2016 and 2015, the Company recognized $1.5 million, $1.4 million and $0.8 million, respectively, related to the research licenses and research and development services unit of accounting in the Regeneron agreement.

Research and Development Expenses—Research and development expenses are charged to expense as incurred. Research and development expenses include primarily personnel-related costs, stock-based compensation expense, laboratory supplies, consulting costs, external contract research and development expenses, including expenses incurred under agreements with CROs, the cost of acquiring, developing and manufacturing clinical study materials, and overhead expenses, such as rent, equipment depreciation, insurance and utilities. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

The Company estimates preclinical studies and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on the Company's behalf. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. These estimates are based on communications with the third-party service providers and the Company's estimates of accrued expenses and on information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. There have been no significant changes from the Company's original estimates in any of the periods presented.

The Company received tax credits from the Australian and French governments in connection with certain research costs incurred in conducting research by the Company's Australian and French subsidiaries. These refunds do not depend on the taxable income or tax position of the Company and therefore the Company does not account for them under an income tax accounting model. The Company recognizes such tax credits in the period when qualified expenses are incurred as a reduction of research expenses. The Company has recorded the reimbursement of $0.1 million, $0.3 million and $0.1 million from the tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss in the years ended December 31, 2017, 2016 and 2015, respectively.

Fair Value Measurements—Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The carrying amounts of the Company's financial instruments, including cash equivalents, prepaid and other current assets, accounts payable, accrued expenses and other current liabilities approximate their fair values due to their short-term maturities. Refer to Note 6 for the methodologies and assumptions used in valuing financial instruments.

Stock-Based Compensation Expense—Stock-based compensation expense related to stock awards to employees is measured at fair value of the award on the date of the grant. The Company estimates the grant-date fair value, and the resulting stock-based compensation expense, using the Black-Scholes valuation model for stock options and using intrinsic value, which is the closing price of its common stock on the date of the grant, for the restricted stock units ("RSUs").The fair value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period, which is generally the vesting period. As of January 1, 2017, the Company adopted Accounting Standard Update ("ASU") No. 2016-09 and elected to account for forfeitures as they occur using a modified retrospective transition method, which requires the Company to record cumulative-effect adjustment to accumulated deficit. The Company determined that the impact of this adoption was immaterial and no adjustments were recorded in its consolidated financial statements. Prior to the adoption of ASU No. 2016-09, stock-based compensation expense recognized for the portion of the award that is expected to vest was reduced by an estimated forfeiture rate.

The Black-Scholes valuation model requires the use of following assumptions:

Expected Term—The expected term assumption represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method.

Expected Volatility—Expected volatility is estimated using comparable public companies' volatility for similar terms.

Expected Dividend—The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company has never paid dividends and has no plans to pay dividends.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero-coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Stock-based compensation expense related to awards granted to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. The fair value of non-employee stock options is estimated using the Black-Scholes valuation model with assumptions generally consistent with those used for employee stock options, with the exception of the expected term, which is the remaining contractual life at each measurement date. Refer to Note 13 for more information on assumptions used in estimating stock-based compensation expense.

Income Taxes—The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize its deferred income tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2017 and 2016, the Company has recorded a full valuation allowance on its deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Comprehensive Loss—Comprehensive loss is comprised of net loss and other comprehensive income (loss). Other comprehensive income (loss) consists of foreign currency translation adjustments related to translation of the financial statements of the Company's Australia and France subsidiaries and unrealized gain (loss) on marketable securities. The Company did not have reclassifications from other comprehensive income (loss) to the income (loss) during the years ended December 31, 2017, 2016 and 2015.

Basic and Diluted Net Loss Per Share— Basic net loss per share is calculated by dividing the net loss by the weighted-average number of shares of common stock outstanding for the period. Diluted net loss per share is computed by giving effect to all potential dilutive common stock equivalents outstanding for the period using the treasury stock method. Outstanding stock options, RSUs, ESPP and warrants are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

Recent Accounting Standard Update Not Yet Effective— In May 2014, the Financial Accounting Standards Board ("FASB") issued ASU No. 2014-09, *Revenue from Contracts with Customers* (Topic 606), which supersedes the revenue recognition requirements in ASC 605*, Revenue Recognition*. This ASU is based on the principle that revenue is recognized to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. ASU 2014-09 defines a five-step process to achieve this core principle and, in doing so, it is possible more judgment and estimates may be required within the revenue recognition process than required under existing U.S. GAAP including identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 is required to be adopted, using either of two methods: (i) retrospective to each prior reporting period presented with the option to elect certain practical expedients as defined within ASU 2014-09; or (ii) retrospective with the cumulative effect of initially applying ASU 2014-09 recognized at the date of initial application and providing certain additional disclosures. In July 2015, the FASB voted to approve a one-year deferral of the effective date to December 15, 2017 for interim and annual reporting periods beginning after that date and permitted early adoption of the standard, but not before the original effective date of December 15, 2016. The FASB issued supplemental adoption guidance and clarification to ASU 2014-09 in March 2016, April 2016, May 2016, December 2016 and November 2017 within ASU 2016-08 *Revenue From Contracts With Customers: Principal vs. Agent Considerations*, ASU 2016-10 *Revenue From Contracts with Customers: Identifying Performance Obligations and Licensing*, ASU 2016-12 *Revenue from Contracts with Customers: Narrow-Scope Improvements and Practical Expedients*, ASU 2016-20 *Technical Corrections and Improvement to Topic 606 – Revenue from Contracts with Customers* and ASU 2017-14 *Reporting Comprehensive Income (Topic 220), Revenue Recognition (Topic 605), and Revenue from Contracts with Customers (Topic 606),* respectively. The Company will adopt the new standard in the first quarter of 2018 using the retrospective approach noted in (ii) above. The Company concluded that its collaboration agreements with Regeneron and Editas will be impacted by the adoption of the new revenue standards. The Company is in the process of allocating the transaction price to the performance obligations in each of the contracts. Preliminarily, the Company anticipates a material impact to its accounting policies, business processes, internal controls and disclosures.

In January 2016, the FASB issued ASU No. 2016-01, *Recognition and Measurement of Financial Assets and Financial Liabilities*, which amends the current guidance on the classification and measurement of financial instruments. Although this ASU retains many current requirements, it significantly revises an entity's accounting related to (i) the classification and measurement of investments in equity securities and (ii) the presentation of certain fair value changes for financial liabilities measured at fair value. This ASU also amends certain disclosure requirements associated with the fair value of financial instruments. The new standard is effective for fiscal years and interim periods within those fiscal years beginning after December 15, 2017, with early adoption permitted for certain changes. This ASU will be effective for the Company in the first quarter of 2018 and must be adopted using a modified retrospective approach, with certain exceptions. The adoption of this standard is not expected to have a significant impact on the Company's consolidated financial statements and related disclosures.

In February 2016, the FASB issued ASU No. 2016-2, *Leases*, which amends the current guidance on leasing activities to provide more transparency and comparability, and requires that all leases be recognized by lessees on their balance sheet as a right-of-use asset and corresponding lease liability, which are currently accounted for as operating leases. The new standard is effective for fiscal years and

interim periods within those fiscal years beginning after December 15, 2018, with early adoption permitted. This ASU will be effective for the Company in the first quarter of 2019 and must be adopted using a modified retrospective transition approach. The Company has not yet determined whether it will elect early adoption and is currently evaluating the impact of the adoption of this standard on its consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU No. 2016-13 *Measurement of Credit Losses on Financial Instruments*. This ASU requires measurement and recognition of expected credit losses for financial assets held. The new standard is effective for fiscal years beginning after December 15, 2019 and interim periods within those fiscal years, with early adoption permitted beginning in the first quarter of 2019. This ASU will be effective for the Company in the first quarter of 2020 and must be adopted using a modified retrospective approach, with certain exceptions. The Company has not yet determined whether it will elect early adoption and is currently evaluating the impact of the adoption of this standard on its consolidated financial statements and related disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*, which clarifies the presentation and classification of certain cash receipts and cash payments in the statement of cash flows. This ASU is effective for annual reporting periods beginning after December 15, 2017, and interim periods within that reporting period. Early adoption is permitted. This ASU will be effective for the Company in the first quarter of 2018. The Company is currently evaluating the impact of the adoption of this standard on its consolidated financial statements and related disclosures.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*, which provides amendments to current guidance to address the classification and presentation of changes in restricted cash in the statement of cash flows. This ASU is effective for annual reporting periods beginning after December 15, 2017, and interim periods within that reporting period. Early adoption is permitted. This ASU will be effective for the Company in the first quarter of 2018. The Company is currently evaluating the impact of the adoption of these standards on its consolidated financial statements and related disclosures.

In May 2017, the FASB issued ASU No. 2017-09, *Scope of Modification Accounting*, which provides amendments to the current guidance for modification accounting. This ASU clarifies that an entity should account for the effects of a modification unless all the following criteria are met: (1) the fair value of the modified award is the same as the fair value of the original award immediately before the original award is modified, (2) the vesting conditions of the modified award are the same as the vesting conditions of the original award immediately before the original award is modified, and (3) the classification of the modified award as an equity instrument or a liability instrument is the same as the classification of the original award immediately before the original award is modified. This ASU is effective for annual reporting periods beginning after December 15, 2017, and interim periods within that reporting period. Early adoption is permitted. This ASU will be effective for the Company in the first quarter of 2018. The Company is currently evaluating the impact of the adoption of these standards on its consolidated financial statements and related disclosures.

The Company has reviewed other recent accounting pronouncements and concluded they are either not applicable to the business or no material effect is expected on the consolidated financial statements as a result of future adoption.

3. Acquisition of Annapurna

(a) Purchase Price Allocation

On May 11, 2016, the Company completed the acquisition of all outstanding equity interests of Annapurna. Annapurna was a privately held French limited liability company and has two wholly-owned subsidiaries, Annapurna, Inc. in the U.S. and Annapurna Therapeutics Limited in Ireland. Annapurna was a biopharmaceutical company focused on discovering and developing novel gene therapy products for people living with severe rare diseases. The primary reasons for the acquisition were to expand the technology platforms within the Company's research and development portfolio and to apply the Company's resources and expertise in gene vectors development to advance Annapurna's programs through development and clinical trials. Annapurna's results of operations and fair value of assets acquired and liabilities assumed are included in the Company's consolidated financial statements from the date of acquisition.

The purchase price consideration was approximately $64.8 million based on the Company's common stock closing price on Nasdaq on the acquisition closing date of $4.14 per share. A total of 14,087,246 shares of the Company's common stock were issued to shareholders of Annapurna in exchange for all common and preferred stock outstanding at the closing date. Annapurna stockholders did not receive any fractional shares of the Company's common stock in connection with the acquisition. Instead of receiving any fractional shares, each Annapurna stockholder was paid an amount in cash (without interest) equal to such fraction amount multiplied by the average 10 business days sale price of the Company's common stock on Nasdaq from the acquisition date. Annapurna Series O preferred shares issued to founders were canceled prior to the acquisition date and were not included in the purchase price consideration. Vesting of certain of Annapurna's stock options and unvested common shares was accelerated at the closing date. The fair value of stock awards related to the accelerated vesting of stock options and common shares of $0.9 million was excluded from

the purchase price consideration and included in the Company's operating expenses post acquisition. A portion of the purchase price was attributed to the exchange of Annapurna's stock options and other rights to purchase capital stock outstanding at the acquisition closing date for corresponding common stock options of the Company at an exchange ratio of 9.54655.

The Company reserved 3,673,940 shares for the future exercise of the Annapurna stock awards assumed in the acquisition. The total fair value of assumed Annapurna stock awards was approximately $14.7 million on the acquisition date, using the Black-Scholes option pricing model, assuming no dividends, expected volatilities of 80% and 89%, risk-free interest rates of 1.4% and 1.1%, and expected lives of six and ten years for employee and non-employee stock awards, respectively. Of the total fair value, $7.4 million was attributed as pre-acquisition service and included as part of the total purchase price consideration. The post-combination attribution amount of $7.2 million is recognized as compensation expense over the remaining requisite service period. The Company included $0.9 million in stock-based compensation expense related to the day-one post combination compensation expenses related to the accelerated vesting of stock options during the second quarter of 2016.

Total purchase price consideration was estimated as follows (in thousands):

Fair value of common shares issued	$ 58,321
Fair value of the Company's common share options exchanged for Annapurna stock options and other stock awards attributable to pre-combination services	7,422
Less: value of common stock and accelerated vesting of stock options at close date	(898)
Total purchase price consideration	$ 64,845

The transaction was accounted for using the acquisition method under ASC 805, *Business Combinations,* with Adverum identified as the acquirer, based on the existence of a controlling financial interest of the combined entities. Under the acquisition method, assets acquired and liabilities assumed were recorded at their estimated fair values as of May 11, 2016. Goodwill, as well as intangible assets that do not qualify for separate recognition, is measured as of the acquisition date as the excess of consideration transferred, which is also measured at fair value, and the net of the fair values of the assets acquired and the liabilities assumed as of the acquisition closing date. Goodwill represents expected synergies of two combined companies. Acquisition costs of $2.5 million were expensed as incurred and recorded as general and administrative expenses in the Company's consolidated statement of operations and comprehensive loss during the year ended December 31, 2016.

The allocation of total purchase price consideration is as follows (in thousands):

Cash	$ 3,449
Prepaid expenses and other assets	865
Property and equipment	185
Acquired intangible assets	16,200
Goodwill	49,514
Accounts payable	(1,118)
Accrued liabilities	(1,848)
Other noncurrent liabilities	(377)
Deferred tax liabilities	(2,025)
Total purchase price allocation	$ 64,845

The identifiable intangible assets acquired consist of IPR&D assets related to products in development, as summarized in the table below (in thousands):

Alpha-1 antitrypsin deficiency ("A1AT"),or ADVM-043	$ 11,700
Hereditary angioedema ("HAE"), or ADVM-053	4,500
Total acquired IPR&D intangible assets	$ 16,200

The fair value of each IPR&D asset was estimated using the income approach and calculated using cash flow projections adjusted for inherent risks regarding regulatory approval, promotion, and distribution, discounted at a rate of approximately 11.0%. The Company acquired two additional intangible assets relating to the Friedreich's Ataxia ("FA") and severe allergy programs, but the fair value of each of these assets was determined to be nominal and was not included in the total acquired intangible assets. All IPR&D intangible assets acquired are classified as indefinite-lived and are not currently being amortized. Acquired IPR&D assets were impaired in the fourth quarter 2016 (see below discussion).

Goodwill, which represents the excess of the purchase price over the fair values assigned to the net assets acquired, was $49.5 million on the acquisition date. The full amount of the goodwill was assigned to the entire Company, since management determined that the Company has only one reporting unit. The goodwill is not deductible for tax purposes. During the year ended December 31, 2016, the Company's goodwill was fully impaired (see below discussion).

The amount of net loss of Annapurna included in the consolidated statements of operations and comprehensive loss from the acquisition date through the period ended December 31, 2016 was $16.6 million, which included $11.2 million of impairment charges related to IPR&D assets. Annapurna did not generate any revenues prior or post acquisition.

The pro forma financial information combines the results of operations of Adverum and Annapurna as though the businesses had been combined as of the beginning of fiscal 2015. The pro forma financial information is presented for informational purposes only, and is not indicative of the results of operations that would have been achieved in the current or any future periods. The following table presents the unaudited pro forma combined results of operations (in thousands, except per share data).

	Years ended December 31,	
	2016	2015
Pro forma information		
Collaboration and license revenue	$ 1,455	$ 2,319
Net loss	$ (117,551)	$ (61,774)
Basic and diluted loss per share	$ (2.85)	$ (1.56)
Weighted-average common shares outstanding - basic and diluted	41,288	39,566

Pro-forma adjustments included the following:

- Actual acquisition-related transaction costs of $2.5 million for year ended December 2016 were excluded from the 2016 pro forma results above. As these expenses were incurred prior to the closing of the acquisition, they were not included in the 2015 pro forma results.
- $0.9 million of stock-based compensation expense related to the accelerated vesting associated with the Annapurna acquisition was excluded from the 2016 pro forma results and was, instead, included in the 2015 pro forma results.
- Stock-based compensation expense of $0.2 million and $0.4 million related to stock options granted to executives upon the closing of the Annapurna acquisition was included in the 2016 and 2015 pro forma results, respectively.
- Interest expense related to convertible notes and changes in fair value of preferred stock warrants of $0.5 million for the year ended December 31, 2015 and $1.0 million for the year ended December 31, 2016, were excluded from 2015 and 2016 pro-forma results above, as the convertible notes and warrants were settled prior to the closing of the Annapurna acquisition.
- Bonuses of $0.4 million paid in connection with closing of the Annapurna acquisition were excluded from the 2016 pro forma results and were, instead, included in the 2015 pro forma results.

The unaudited condensed pro forma information does not include any anticipated synergies that may be achievable subsequent to the date of acquisition.

b) Impairment Evaluation for Goodwill and Intangible Assets

As the Company recorded goodwill and IPR&D intangible assets upon the Annapurna acquisition, the Company is required to test goodwill and indefinite lived intangible assets for impairment on an annual basis or more frequently if indicators of impairment exist. The Company operates as one reporting unit and goodwill was allocated to this reporting unit.

During the second quarter of 2016, the Company noted a continuing decrease in its stock price that resulted in the market capitalization being less than the carrying value of the Company's net assets as of June 30, 2016. As the operating losses were expected to increase significantly in the following years due to continuing pre-clinical and expected clinical trials, the Company concluded that it was more likely than not that the fair value of the Company's one reporting unit was less than its carrying value and, as a result, performed a step one goodwill impairment analysis.

In performing the step one analysis, the Company determined the fair value of the reporting unit using a market-based approach. The Company multiplied the stock price of $3.16 by the 41.3 million of its common shares outstanding on June 30, 2016 and applied a control premium to estimate the common equity value on a controlling basis. As the fair value was less than the carrying value of the Company's net assets, the Company proceeded to step two of the impairment analysis.

The second step of the analysis includes allocating the calculated fair value (determined in the step one analysis) of the reporting unit to its assets and liabilities to determine an implied fair value of goodwill. The implied fair value of goodwill was determined in the same manner as the amount of goodwill recognized in an acquisition. That is, the estimated fair value of the reporting unit was allocated to all of the assets and liabilities as if the Company had been acquired and the estimated fair value was the purchase price paid. As part of this assessment the Company considered the preliminary valuation of Annapurna net assets acquired, excluding goodwill, as their fair value from May 11, 2016, the acquisition closing date, to June 30, 2016 did not change. The Company also noted that the fair value of current assets and liabilities approximated their carrying value due to their short-term nature, the Company's cash and cash equivalent balance was higher than the fair value estimated in the step one analysis, and the fair value of fixed assets approximated their recorded value as most of the Company's fixed assets were acquired in the last couple of years. Based on this analysis, the implied fair value of the goodwill was zero. Accordingly, the Company fully impaired its goodwill and recorded an impairment charge was $49.5 million, which is included within impairment of goodwill and intangible assets in the Company's consolidated statements of operations and comprehensive loss for the year ended December 31, 2016.

In the fourth quarter of 2016, the Company performed its annual impairment assessment of its intangible assets, ADVM-043 and ADVM-053. Based on the Company's decision in the fourth quarter to change its manufacturing process for ADVM-043 and ADVM-053 by implementing its proprietary baculovirus-based production system, it updated the related development and manufacturing costs. As a result, the Company revised its forecasts for manufacturing and related costs. In addition, the Company also reviewed and updated its expected timing of clinical trials, receipts of regulatory approvals and costs to complete. Based upon the Company's analysis, it determined that the total carrying value of $16.2 million for its intangible assets, ADVM-043 and ADVM-053, was higher than their total fair value of $5.0 million. Accordingly, the Company recorded $11.2 million impairment charge. Intangible asset related to ADVM-053 was fully impaired and intangible assets related to ADVM-043 was impaired and had fair value of $5.0 million as of December 31, 2016. Impairment charges for goodwill and intangible assets are included in the Company's consolidated statements of operations and comprehensive loss.

In the fourth quarter of 2017, the Company performed its annual impairment assessment of its intangible asset, ADVM-043. Based on the Company's impairment analysis, it concluded that its ADVM-043 IPR&D asset was not impaired.

4. Restructuring Charges

On December 22, 2015, the Company implemented a restructuring plan to reduce operating costs and better align its workforce with the needs of its business following its decision to not initiate the Phase 2b clinical trial for AVA-101 during the second half of 2015. The plan resulted in a reduction of approximately 20% of the Company's workforce, or a total of 15 employees. Affected employees were eligible to receive severance payments. The plan also triggered accelerated vesting of certain of the affected employees' restricted stock units ("RSUs").

In connection with the restructuring plan, the Company estimated aggregate restructuring charges of approximately $2.6 million, which were recorded in the Company's consolidated statements of operations and comprehensive loss during the year ended December 31, 2015, related to one-time termination severance payments and other employee-related benefits, which included approximately $1.0 million of stock-based compensation expense related to the acceleration of RSUs.

The following table summarizes the restructuring activities (in thousands):

	One-Time Termination Benefits	Non-Cash Charge Related to Acceleration of RSUs	Total
Restructuring liability as of December 31, 2014	$ —	$ —	$ —
Costs incurred and recorded as restructuring charges	1,524	1,049	2,573
Cash payments	(511)	—	(511)
Non-cash settlements	—	(1,049)	(1,049)
Restructuring liability as of December 31, 2015	1,013	—	1,013
Cash payments	(988)	—	(988)
Restructuring liability as of December 31, 2016	25	—	25
Cash payments	(25)	—	(25)
Restructuring liability as of December 31, 2017	$ —	$ —	$ —

5. Cash Equivalents and Short-Term Investments

The following is a summary of the Company's cash equivalents and short-term investments (in thousands):

December 31, 2017	Amortized Cost Basis	Unrealized Gains	Unrealized Loses	Estimated Fair Value
Money market funds	$ 65	$ —	$ —	$ 65
U.S. government and agency securities	58,351	—	(145)	58,206
Commercial paper	71,427	—	—	71,427
Corporate bonds	38,354	1	(38)	38,317
Certificates of deposit	9,731	—	—	9,731
Total cash equivalents and short-term investments	177,928	1	(183)	177,746
Less: Cash equivalents	(57,780)	—	—	(57,780)
Total short-term investments	$ 120,148	$ 1	$ (183)	$ 119,966
December 31, 2016				
Money market funds - cash equivalent	$ 215,916	$ —	$ —	$ 215,916
Total cash equivalents	$ 215,916	$ —	$ —	$ 215,916

Management determined that the gross unrealized losses on the Company's marketable securities as of December 31, 2017 were temporary in nature. Therefore, none of the Company's marketable securities were other-than-temporarily impaired as of December 31, 2017. As of December 31, 2016, all of the Company's investments in marketable securities were held in money market funds and were classified as cash equivalents.

The following table is a summary of the cost and estimated fair value of the Company's marketable securities based on stated effective maturities as of December 31, 2017:

	Amortized Cost Basis	Estimated Fair Value
	(In thousands)	
Mature within one year	$ 169,909	$ 169,758
Mature after one year to three years	8,019	7,988
Total cash equivalents and short-term investments	$ 177,928	$ 177,746

6. Fair Value Measurements and Fair Value of Financial Instruments

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

The fair value of Level 1 securities is determined using quoted prices in active markets for identical assets. Level 1 securities consist of highly liquid money market funds. Financial assets and liabilities are considered Level 2 when their fair values are determined using inputs that are observable in the market or can be derived principally from or corroborated by observable market data such as pricing for similar securities, recently executed transactions, cash flow models with yield curves, and benchmark securities. In addition, Level 2 financial instruments are valued using comparisons to like-kind financial instruments and models that use readily observable market data as their basis. U.S. government and agency securities, commercial paper, corporate bond and certificates of deposit are valued primarily using market prices of comparable securities, bid/ask quotes, interest rate yields and prepayment spreads and are included in Level 2.

In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3 within the valuation hierarchy. Level 3 liabilities that were measured at estimated fair value on a recurring basis consist of a financing arrangement entered during the year ended December 31, 2016.

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at estimated fair value using Level 3 inputs. There were no transfers within the hierarchy during the years ended December 31, 2017 and 2016.

The following table summarizes, for assets and liabilities recorded at fair value, the respective fair value and the classification by level of input within the fair value hierarchy as described above (in thousands):

	Total Carrying Value	Quoted Prices In Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
December 31, 2017				
Assets:				
Money market funds	$ 65	$ 65	$ —	$ —
U.S. government and agency securities	58,206	—	58,206	—
Commercial paper	71,427	—	71,427	—
Corporate bonds	38,317		38,317	
Certificates of deposit	9,731	—	9,731	—
Total cash equivalents and short-term investments	$ 177,746	$ 65	$ 177,681	$ —
Other noncurrent liability:				
Financing arrangement	$ 157	$ —	$ —	$ 157
December 31, 2016				
Assets:				
Money market funds	$ 215,916	$ 215,916	$ —	$ —
Total cash equivalents	$ 215,916	$ 215,916	$ —	$ —
Other noncurrent liability:				
Financing arrangement	$ 74	$ —	$ —	$ 74

In August 2016, the Company entered into a financing arrangement with the TAP for a total amount of up to $0.3 million (the "TAP financing"), of which approximately $0.2 million and $0.1 million, respectively, was outstanding as of December 31, 2017 and 2016 (see Note 10). The Company elected the fair value option to account for this financing arrangement. The fair value of the financing arrangement was determined based on the expected value approach and is classified as Level 3 within the fair value hierarchy. The Company determined that the changes in the fair value were immaterial during the years ended December 31, 2017 and 2016. The key unobservable inputs in the valuation model include timing of milestones, probability of achievement of development and commercial milestones, and a discount factor.

The following table presents quantitative information about the inputs and valuation methodologies used for the fair value measurements classified in Level 3 of the fair value hierarchy:

	Fair Value at December 31,		Valuation	Significant Unobservable	Weighted-Average (range - if applicable) as of December 31,	
	2017	2016	Methodology	Input	2017	2016
	(In thousands)					
TAP financing	$ 157	$ 74	Expected value approach	Milestone dates:	2018 - 2023	2017 - 2023
				Discount rate:	5.8%	5.5%
				Percent probability of milestone achievements:	18.2% to 65.0%	18.2% to 80.0%

Non-financial assets such as intangible assets, property, plant, and equipment are evaluated for impairment and adjusted to their fair value using Level 3 inputs, only when impairment is recognized. Fair values are considered Level 3 when management makes significant assumptions in developing a discounted cash flow model based upon a number of considerations, including projections of revenues, earnings and a discount rate. In addition, in evaluating the fair value of goodwill impairment, further corroboration is obtained using the Company's market capitalization.

7. Significant Agreements

University of California Agreement

In May 2010, the Company entered into a license agreement with the Regents of University of California (the "Regents"), as amended in September 2013. Under the license agreement, the Regents granted to the Company an exclusive (even as to the Regents) license, with the right to grant sublicenses, under the Regents' undivided interest in patent rights covering a method of using recombinant gene delivery vectors, including AAV7m8 in the Company's wet AMD product candidate ADVM-022, for treating or preventing diseases of the eye, to develop, make, have made, use offer for sale, import, export and sell products covered by such patent rights in all fields of use in the U.S. The licensed patent rights are jointly owned by the Regents and Chiron Corporation, which was acquired by Novartis AG, but the Company's license extends only to the Regents' interest in such patent rights.

The Company is obligated to make milestone payments totaling up to $0.9 million upon reaching certain stages of development of the licensed products for one indication, and totaling up to $0.5 million for each subsequent indication for which licensed products are developed, for up to a maximum of two additional indications. Through December 31, 2017, none of these goals had been achieved, and no milestones were payable.

The Company's license agreement with the Regents continues in effect for the life of the last-to-expire patent. The Company expects the agreement to terminate prior to any commercialization of any product candidates to which they apply. The Company may terminate this agreement without cause at any time upon 30 days' prior written notice to the Regents. The Regents may terminate this agreement for a breach by the Company that remains uncured for 60 days, if the Company becomes insolvent, if the Company directly or through a third party files a claim that a licensed patent right is invalid or unenforceable, or if the Company fails to meet or extend the date for meeting certain diligence milestones.

Regeneron Agreement

In May 2014, the Company entered into a research collaboration and license agreement with Regeneron to discover, develop and commercialize novel gene therapy products for the treatment of ophthalmologic diseases. The collaboration covers up to eight distinct therapeutic targets ("collaboration targets"). The Company and Regeneron collaborated during the initial research period of three years. In February 2017, Regeneron exercised its option to extend the research collaboration and license agreement for an additional three years, through May 1, 2020. During the research period, Regeneron has the option to obtain an exclusive worldwide license for a collaboration target's further development by giving written notice to the Company and paying $2.0 million per target. If Regeneron exercises its option, it will be responsible for all further development and commercialization of the target. The Company is then eligible to receive contingent payments of up to $80.0 million upon achievement of certain development and regulatory milestones for product candidates directed toward each collaboration target, for a combined total of up to $640.0 million in potential milestone payments for product candidates directed toward all eight collaboration targets, plus a royalty in the low- to mid-single-digits on worldwide net sales of collaboration products.

For any two collaboration targets, the Company has an option to share up to 35% of the worldwide product candidate development costs and profits. If the Company exercises this option, the Company will not be eligible for milestone and royalty payments as discussed above but rather the Company will share development costs and profits with Regeneron.

The agreement will expire with respect to each collaboration target upon expiration of all payment obligations by Regeneron. In addition, the agreement, or Regeneron's rights to any target development under the agreement, may terminate early under the following situations:

- Regeneron may terminate the agreement for convenience at any time on a target by target basis or in totality upon a 30-day notice.
- Each party can terminate the agreement if another party commits a material breach or material default in performance of its obligations and such breach or default is not cured within 60 days.
- The agreement is automatically terminated upon initiation of any bankruptcy proceedings, reorganization or dissolution of either party.
- The Company can terminate the agreement upon 30-day notice if Regeneron challenges the validity, scope or enforceability of any Company patent.

Under the Company's research, collaboration and license agreement with Regeneron, the Company is required to have a mutually agreed-on research plan with Regeneron in order to invoice Regeneron for services performed. The Company does not currently have a research plan in place, and, consequently, it does not currently receive any reimbursements from Regeneron.

Editas Agreement

In August 2016, the Company entered into a collaboration, option and license agreement with Editas pursuant to which the Company and Editas collaborate on certain studies using AAV vectors in connection with Editas' genome editing technology and the Company grants to Editas an exclusive option to obtain certain exclusive rights to use the Company's proprietary vectors in up to five ophthalmic indications. The Company received a $1.0 million non-refundable upfront payment during the year ended December 31, 2016, with $0.5 million of such payment to be credited against Editas' obligation to fund research and development costs. Under the terms of the agreement, both the Company and Editas are subject to exclusivity obligations. In January 2018, the Company and Editas extended the research collaboration, option and license agreement. In consideration for extending the agreement, Editas made a one-time, non-refundable cash payment of $0.5 million to the Company in February 2018 (see Note 17).

Under the terms of the agreement, as amended, Editas may exercise the option with respect to a designated initial indication until September 30, 2018. With respect to the four other indications, Editas may exercise the option until the fourth anniversary of the effective date, provided that the option will expire on the third anniversary of the effective date if Editas has not exercised the option with respect to the initial indication or any other indication by such date. Upon Editas' timely exercise of the option with respect to the designated initial indication, Editas will pay the Company a $1.3 million fee. For the first additional indication for which Editas timely exercises its option, Editas will pay the Company a $1.5 million fee. Upon each subsequent exercise of the option, Editas will pay the Company a $1.0 million fee per Indication. If Editas elects to develop a product using certain of the Company's proprietary vectors, the Company will be eligible to receive up to $15.5 million in development and commercialization milestone payments for such product, and tiered royalties between the mid-single digits and low teens on net sales of such product, subject to certain adjustments.

Unless earlier terminated, the agreement will be in effect until the later of the expiration of the option exercise period or the expiration of the royalty term of the last product. At any time after the option is first exercised, Editas may terminate the agreement for convenience in its entirety or on an indication-by indication or country-by-country basis, upon prior written notice to the Company. The Company may also terminate the agreement if Editas challenges the Company's patents relating to its proprietary vectors and does not withdraw such challenge within a defined period of time. In addition, either party may terminate the agreement with written notice upon a bankruptcy of the other party or upon an uncured material breach by the other party.

Cornell University Agreement

The Company had been a party to a master service agreement (the "MSA") with Cornell University ("Cornell") originally established in August 2014 and amended in December 2015. Under the MSA, Cornell provided assistance in regulatory affairs, overall project management, and parameter development. Subsequent to the Annapurna acquisition, the Company recorded a total research and development expenses of $1.8 million related to Cornell agreements for the year ended December 31, 2016.

In December 2016, the Company informed Cornell that the Company decided to terminate the MSA for material breach, effective January 6, 2017. Subsequently, Cornell informed the Company that it disputes the validity of the Company's termination of the MSA. Although the Company intends to defend the validity of its termination of the MSA, the Company recorded $2.0 million of estimated costs associated with the termination of the MSA as of December 31, 2017. The MSA included services relating to the Company's gene therapy programs ADVM-043, ADVM-053 and severe allergy. The Company's three licensing agreements with Cornell for these programs remain unchanged.

The decision to terminate the MSA was due to Cornell's failure to deliver therapeutic material of ADVM-043 suitable for use in human patients. As a result of this decision, the Company contracted with large-scale contract manufacturing organizations that comply with current good manufacturing practice industry standards and can produce product quantities for both the Company's planned clinical trials and potential commercial supply. This is part of the Company's upgrade of the manufacturing process for ADVM-043.

In December 2015, the Company entered into three licensing agreements with Cornell, pursuant to which the Company will advance its gene therapy programs ADVM-043, ADVM-053, and severe allergy, which originally were initiated at the Department of Genetic Medicine at Weill Cornell.

A1AT Deficiency License Agreement—Under this agreement, the Company holds an exclusive license to certain know-how related to A1AT deficiency and rights to an Investigational New Drug (IND) application to initiate clinical studies of gene therapy for A1AT.

HAE License Agreement—Under this agreement, the Company holds an exclusive license to certain technology related to hereditary angioedema (HAE) and a non-exclusive license to certain other intellectual property related to the HAE program.

Allergy License Agreement—Under this agreement, the Company holds an exclusive license to certain patents related to allergens and a non-exclusive license to certain other technology related to allergens.

Across these three license agreements, Cornell is entitled to receive aggregate annual maintenance fees ranging from $30,000 to $0.3 million per year, up to $16.0 million in aggregate milestone payments and royalties on sales in the low single-digits, subject to adjustments and minimum thresholds. For the year ended December 31, 2017 and 2016, annual maintenance fees were immaterial. No milestone payments were probable to achieve and none were recorded as of December 31, 2017 and 2016.

Dr. Crystal, Chairman of Genetic Medicine, the Bruce Webster Professor of Internal Medicine and a Professor of Genetic Medicine and of Medicine at Weill Cornell, served as a consultant to the Company since the inception of Annapurna and continues to provide services for annual base compensation of $0.2 million.

REGENXBIO Agreement

A1AT Deficiency/Allergy License Agreement—In October 2015, the Company entered into an exclusive worldwide license to certain intellectual property in order to make, have made, use, import, sell and offer for sale certain licensed products for the treatment of A1AT deficiency. Under this agreement, the Company has an option to be granted an exclusive worldwide license to certain intellectual property related to the treatment of severe allergies, which option expired in October 2016. Also, under this license agreement, REGENXBIO, Inc. ("REGENXBIO") is eligible to receive annual maintenance fees, up to approximately $20.0 million in combined milestone payments and royalties in the mid-to-high single digits.

In April 2017, the Company exercised its right to terminate the license agreement for any reason upon six months' prior written notice. The termination was effective in October 2017.

FA License Agreement—In April 2014, the Company entered into an exclusive worldwide license to certain intellectual property related to the FA program to make, have made, use, import, sell and offer for sale licensed products using AAVrh10 for FA where the vector is administered by any route except directly to the central nervous system ("FA Systemic"). Under the terms of this license agreement, the Company also had an option to obtain a non-exclusive worldwide license to make, have made, use, import, sell and offer for sale licensed products using a single vector for each of FA where the vector is administered directly to the central nervous system ("FA CNS") and FA Systemic. Under this license agreement, REGENXBIO is eligible to receive annual maintenance fees, up to $13.9 million in combined milestone fees and royalties in the mid-to-high single digits. The option to obtain a non-exclusive license to FA Systemic expired in April 2015 and the option to obtain a non-exclusive license for FA CNS expired in April 2016. The Company is obligated to achieve certain development milestones with respect to each licensed disease indication, including the filing of an IND application for each licensed disease indication within a specified time period, which it may extend for additional time for a specified number of extensions upon the payment of a fee. In October 2017, the Company notified REGENXBIO that the Company exercised its right to terminate this license agreement for any reason upon six months' written notice. The termination will be effective in April 2018.

Inserm Transfert

In July 2014, the Company entered into an agreement with Inserm Transfert ("Inserm") whereby it holds an exclusive license to certain patents to develop, make, have made, use, import, offer for sale and sell or otherwise distribute products for the treatment of FA and a non-exclusive license to certain other intellectual property related to the FA program. The agreement was amended in October 2015 to increase the scope of the intellectual property under the licenses. Under this agreement, Inserm is entitled to receive certain de minimis license payments, certain development milestone payments of up to approximately €2.0 million in the aggregate and royalties on sales in the low single-digits, subject to adjustments. No milestone payments were probable to achieve and none were recorded as of December 31, 2017.

Unless earlier terminated, this agreement will be in effect on a country-by-country, licensed product-by-licensed product basis until the later of the expiration of the last claim of the licensed intellectual property which cover the manufacture, use or sale of such product in such country or 10 years after the first commercial sale of such product in such country in which such product is sold. Upon a country-by-country and product-by-product basis, the Company will have a fully paid up, perpetual, irrevocable license with respect to such product in such country under the licensed intellectual property following expiration of this agreement with respect to such product in the applicable country. The Company may terminate this agreement upon 60 days' prior written notice. Inserm may terminate this license agreement if the Company becomes the subject of a voluntary or involuntary petition in bankruptcy or fails to

meet development milestones and such failure is not cured within a specified number of days. Inserm may also terminate the license granted to the Company in a given country if the Company (i) before regulatory approval of a product in any country, has ceased conducting any development of products in all countries for 12 consecutive months or (ii) after regulatory approval of a product in a given country, has ceased marketing such product in such country for 12 consecutive months.

Pursuant to the terms of the agreement with Inserm, due to the acquisition of Annapurna, the Company made a one-time payment of €0.3 million to Inserm during the year ended December 31, 2017.

8. Property and Equipment, Net

Property and equipment, net consists of the following:

	December 31,	
	2017	2016
	(In thousands)	
Computer equipment and software	$ 535	$ 300
Laboratory equipment	4,956	4,285
Furniture and fixtures	552	552
Leasehold improvements	1,549	1,522
Construction in progress	105	104
Total property and equipment	7,697	6,763
Less accumulated depreciation and amortization	(4,673)	(2,594)
Property and equipment, net	$ 3,024	$ 4,169

Depreciation and amortization expense related to property and equipment was $2.1 million, $1.6 million and $0.8 million for the years ended December 31, 2017, 2016 and 2015, respectively.

9. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2017	2016
	(In thousands)	
Employees' compensation	$ 2,259	$ 2,570
Accrued preclinical costs	1,255	1,683
Accrued professional fees	2,295	894
Accrued clinical and process development costs	910	1,142
Other	245	187
Total accrued expenses and other current liabilities	$ 6,964	$ 6,476

10. Financing Arrangements

Banque Publique d'Investissement ("BPI France") Agreement

In August 2015, BPI France granted Annapurna a €0.8 million interest-free conditional advance, of which €0.5 million was outstanding as of December 31, 2016. Payments are scheduled in equal quarterly amounts of €25,000 from September 30, 2017 to June 30, 2022. This payment schedule will be modified if the Company will receive revenue from license or product sales before advances are paid in full. The Company calculated 7% imputed interest expense on these advances that was recorded as a discount at the issuance date. The discount is amortized as an interest expense over the life of the advances. As of December 31, 2017 and 2016, the total carrying value, which approximates the fair value, of the conditional advance was $0.4 million, of which $0.3 million was recorded within other non-current liabilities and $0.1 million within accrued expenses and other current liabilities in the Company's consolidated balance sheets.

The TAP Agreement

In July 2016, the Company entered into a sponsored research agreement with The TAP in which the TAP will fund the Company's A1AT research activities of up to $0.3 million in cash in three different tranches. The Company may repay up to 4.5 times the received amount if and when certain product approval and sales milestones are achieved. In September 2016, the Company received $0.1 million and issued warrant to purchase 10,000 shares of its common stock exercisable anytime during five years from the issuance date at an exercise price of $4.33 per share (the "TAP warrant). In December 2017, the Company achieved a milestone which entitled the Company to receive $0.1 million. For the valuation details of the TAP financing, refer to Note 6.

The following table presents the TAP financing activity:

	Years ended December 31,	
	2017	2016
	(In thousands)	
Balance of TAP financing liability as of the beginning of the year (1)	$ 74	$ —
Funding (2)	100	100
Fair value of common stock warrant issued (see Note 12) (3)	—	(26)
Gain on fair value of TAP financing liability (4)	(17)	—
Balance of TAP financing liability as of the end of the year	$ 157	$ 74

(1) Recorded within other non-current liabilities in the Company's consolidated balance sheets.
(2) Recorded as a receivable as of December 31, 2017. Payment was received in January 2018.
(3) Recorded within other non-current liabilities and additional paid-in capital in the Company's consolidated balance sheets.
(4) Recorded within other non-current liabilities in the Company's consolidated balance sheet and other income, net in the Company consolidated statement of operations and comprehensive loss.

11. Commitments and Contingencies

Facility Lease Agreement

The Company leases its' office building under a non-cancelable lease agreement, which expires on May 8, 2020. The Company may extend this lease for up to four years. The lease agreement provides for an escalation of rent payments each year. The Company records rent expense on a straight-line basis over the term of the lease.

As of December 31, 2017, future minimum commitments under the Company's facility operating lease were as follows:

Years ended December 31,	Future Commitments
	(In thousands)
2018	$ 1,162
2019	1,197
2020	403
Total minimum lease payments	$ 2,762

Rent expense recognized under the operating lease, including additional rent charges for utilities, parking, maintenance, and real estate taxes was $1.8 million, $1.7 million and $1.5 million for the years ended December 31, 2017, 2016 and 2015, respectively.

Contractual Obligations

As of December 31, 2017, the Company had a contractual obligation of approximately $4.2 million for a contract manufacturing with a vendor for materials production related to our three programs, ADVM-022, ADVM-043 and ADVM-053.

Collaborations and License Agreements

The Company is a party to various agreements, principally relating to licensed technology that requires future payments relating to milestones or royalties on future sales of specified products. Through December 31, 2017, none of the goals had been achieved under the license agreements and no milestones were accrued or payable. Because the achievement of these milestones is not fixed and determinable, such commitments have not been included on the Company's consolidated balance sheets. Aggregate annual maintenance fee's payments were approximately $0.5 and $0.6 million for each of the years ended December 31, 2017 and 2016.

Guarantees and Indemnifications

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for indemnification for certain liabilities. The exposure under these agreements is unknown because it involves claims that may be made against the Company in the future but have not yet been made. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. However, the Company may record charges in the future as a result of these indemnification obligations. The Company also has indemnification obligations to its directors and executive officers for specified events or occurrences, subject to some limits, while they are serving at the Company's request in such capacities. There have been no claims to date and the Company believes the fair value of these indemnification agreements is minimal. Accordingly, the Company has not recorded any liabilities for these agreements as of December 31, 2017 and 2016.

Legal Proceedings

From time to time, the Company may become involved in litigation and other legal actions. The Company estimates the range of liability related to any pending litigation where the amount and range of loss can be estimated. The Company records its best estimate of a loss when the loss is considered probable. Where a liability is probable and there is a range of estimated loss with no best estimate in the range, the Company records a charge equal to at least the minimum estimated liability for a loss contingency when both of the following conditions are met: (i) information available prior to issuance of the financial statements indicates that it is probable that a liability had been incurred at the date of the financial statements and (ii) the range of loss can be reasonably estimated.

In July 2015, three securities class action lawsuits were filed against the Company and certain of its officers in the United States District Court for the Northern District of California ("U.S. District Court"), each on behalf of a purported class of persons and entities who purchased or otherwise acquired the Company's publicly traded securities between July 31, 2014 and June 15, 2015. The lawsuits assert claims under the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Securities Act of 1933, as amended (the "Securities Act") and allege that the defendants made materially false and misleading statements and omitted allegedly material information related to, among other things, the Phase 2a clinical trial for AVA-101, a product candidate which is no longer being developed, and the prospects of AVA-101. The complaints seek unspecified damages, attorneys' fees and other costs.

In December 2015, a putative securities class action lawsuit was filed against the Company, the Company's board of directors, underwriters of the Company's January 13, 2015, follow-on public stock offering, and two of the Company's institutional stockholders, in the Superior Court of the State of California for the County of San Mateo ("San Mateo Superior Court"). The complaint alleges that, in connection with the Company's follow-on stock offering, the defendants violated the Securities Act by allegedly making materially false and misleading statements and by allegedly omitting material information related to the Phase 2a clinical trial for AVA- 101 and the prospects of AVA-101. The complaint seeks unspecified compensatory and rescissory damages, attorneys' fees and other costs. The plaintiff has dismissed the two institutional stockholder defendants.

On March 16, 2017, the Company reached an agreement to settle the asserted actions. The proposed aggregate amount of the settlement is $13.0 million, of which $1.0 million would be contributed by the Company to cover its indemnification obligations to the underwriters, and the remainder would be contributed by the Company's insurers. The Company and the defendants have denied and continue to deny each and all of the claims alleged in the actions, and the settlement does not assign or reflect any admission of fault, wrongdoing or liability as to any defendant. Notice of the settlement was provided to shareholders in the fall of 2017, and no shareholder objected to the settlement. On January, 19, 2018, the San Mateo Superior Court entered a judgment and order finally approving the settlement. And on February 5, 2018, the U.S. District Court entered an order dismissing the consolidated federal action with prejudice. If the settlement does not become effective and litigation resumes, following an appeal or otherwise, adverse outcomes in the actions could result in substantial damages. The Company recorded $1.0 million as general and administrative expense during the three months ended March 31, 2017, when the amount and time of settlement became estimable and probable.

12. Stockholders' Equity

Common Stock and Preferred Stock

The Company's authorized share capital is 300,000,000 shares of common stock and 5,000,000 shares of preferred stock. As of December 31, 2017 and 2016, the Company had no preferred stock issued and outstanding.

Common Stock Warrants

The Lions Eye Institute ("LEI") Warrants. In connection with the Company's research and collaboration agreement, as amended, with LEI (the "LEI Agreement"), the Company agreed to issue a warrant to purchase a certain number of the Company's common stock upon the achievement of each milestones as set forth in the LEI Agreement.

During the year ended December 31, 2015, the Company issued a warrant to purchase 40,000 shares of its common stock with an exercise price of $10.51 per share to LEI. This common stock warrant is exercisable immediately, and expires on October 15, 2020. The estimated the fair value of this warrant was approximately $0.2 million and was recorded within research and development expenses in the Company's consolidated statement of operations and comprehensive loss and additional paid-in capital in the Company's consolidated balance sheet for the year ended December 31, 2015. The fair value of the warrant was calculated using the Black-Scholes valuation model, and was based on the closing price of common stock on the issuance date of $8.35 per share, contractual term of the warrant of 5 years, a risk-free interest rate of 1.34%, an expected volatility of 75% and a 0% expected dividend yield.

Additionally, in September 2017, the Company issued a warrant to purchase 40,000 shares of its common stock with an exercise price of $3.65 per share to LEI. This common stock warrant is exercisable immediately, and expires on September 29, 2022. The estimated the fair value of this warrant was approximately $0.1 million and the fair value of this warrant was recorded as research and development expenses in the Company's consolidated statement of operations and comprehensive loss and additional paid-in capital in the Company's consolidated balance sheet for the year ended December 31, 2017. The fair value of the warrant was calculated using the Black-Scholes valuation model, and was based on the closing price of common stock on the issuance date of $3.65 per share, contractual term of the warrant of 5 years, a risk-free interest rate of 1.89%, an expected volatility of 91% and a 0% expected dividend yield.

TAP Warrant. In July 2016, in connection with the TAP financing agreement (see Note 10), the Company issued a warrant to purchase 10,000 shares of its common stock exercisable anytime during five years from the issuance date at an exercise price of $4.33 per share. The estimated fair value of this warrant was $26,000 at the issuance date using the Black-Scholes valuation model with the following assumptions: exercise price of $4.33 per share, expected term of the warrant of 5 years, a risk-free interest rate of 1.07%, an expected volatility of 72% and a 0% expected dividend. The fair value of TAP warrant was recorded to non-current liabilities and additional paid-in-capital in the Company's consolidated balance sheet for the year ended December 31, 2016.

13. Stock Plans

On December 26, 2006, the Company adopted the 2006 Equity Incentive Plan, which was amended by the board of directors on November 15, 2012 (the "2006 Plan"). The 2006 Plan allowed for the granting of incentive stock options ("ISOs") and non-qualified stock options ("NSOs") to the employees, members of the board of directors and consultants of the Company. ISOs were granted only to the Company's employees, including officers and directors who are also employees. NSOs were granted to the employees and consultants. In July 2014, the Company's board of directors and its stockholders approved the establishment of the 2014 Equity Incentive Award Plan (the "2014 Plan"). Options may no longer be issued under the 2006 Plan after July 30, 2014. In addition, the 2014 Plan provides for annual increases in the number of shares available for issuance thereunder on the first business day of each fiscal year, beginning with the year ended December 31, 2015, equal to four percent (4%) of the number of shares of the Company's common stock outstanding as of such date or a lesser number of shares as determined by the Company's board of directors.

In October 2017, the Company adopted the 2017 Inducement Plan (the "Inducement Plan"). The Company reserved 600,000 shares for issuance pursuant to stock options and RSUs under the Inducement Plan. The only persons eligible to receive grants of stock options and RSUs under Inducement Plan are individuals who satisfy the standards for inducement grants under Nasdaq guidance that is, generally, a person not previously an employee or director of Adverum, or following a bona fide period of non-employment, as an inducement material to the individual's entering into employment with Adverum.

The 2006 Plan, 2014 Plan and Inducement Plan are referred to collectively as the Plans. As of December 31, 2017, a total of 17,167,856 shares of common stock were reserved for issuance and 2,830,010 shares were available for future grants under the Plans.

Stock Options

Stock options under the 2014 Plan and the Inducement Plan may be granted for periods of up to 10 years and at prices no less than 100% of the estimated fair value of the shares on the date of grant as determined by the board of directors, provided, however, that the exercise price of an ISO and NSO granted to a 10% stockholder may not be less than 110% of the estimated fair value of the shares on the date of grant. Stock options granted to employees and non-employees generally vest ratably over four years.

The following table summarizes stock option activity under the Company's stock plans and related information:

(In thousands, except exercise prices and years)	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contract Life (in years)	Aggregate Intrinsic Value (a)
Balance at December 31, 2016	7,449	$ 4.46	8.4	$ 11,837
Granted	1,989	2.85		
Exercised	(1,808)	0.20		
Cancelled/forfeited	(935)	8.87		
Balance at December 31, 2017	6,695	$ 4.51	7.4	$ 9,539
Vested and expected to vest as of December 31, 2017	6,695	$ 4.51	7.4	$ 9,539
Exercisable at December 31, 2017	3,202	$ 4.96	6.1	$ 6,207

(a) The aggregate intrinsic value is calculated as the difference between the stock option exercise price and the closing price of the Company's common stock of $3.5 per share as of December 31, 2017.

In June 2017 and 2016, the Company granted 150,000 stock options and 518,000 stock options, respectively, outside the Plans to its certain executive officers. In December 2015, the Company granted 910,000 stock options outside of the Plans to its new Principal Executive Officer.

The total intrinsic value of stock options exercised during the years ended December 31, 2017, 2016 and 2015 were $4.8 million, $7.1 million and $11.2 million, respectively.

Stock Options Granted to Employees. The fair value of each stock option issued to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	Options			Employee Stock Purchase Plan		
	Years ended December 31,			Years ended December 31,		
	2017	2016	2015	2017	2016	2015
Expected volatility	82%	81%	79%	52%	70%	74%
Expected term (in years)	6.0	6.1	6.1	0.5	0.5	0.5
Expected dividend yield	—	—	—	—	—	—
Risk-free interest rate	1.9%	1.8%	1.7%	1.3%	0.6%	0.1%

The weighted-average fair values of options granted during the years ended December 31, 2017, 2016 and 2015 were $1.99, $3.35 and $15.91, respectively.

As of December 31, 2017, there was $8.9 million of unrecognized stock-based compensation expense related to employee stock options that is expected to be recognized over a weighted-average period of 2.2 years.

Stock Options Granted to Non-Employees. Stock-based compensation expense related to stock options granted to non-employees is recognized as the stock options are earned. The Company believes that the estimated fair value of the stock options is more readily measurable than the fair value of the services rendered.

The following table presents the weighted-average assumptions used in the Black-Scholes valuation model to estimate the fair value of non-employee stock options:

	Years ended December 31,		
	2017	2016	2015
Expected volatility	84%	82%	81%
Expected term (in years)	8.8	9.1	3.3
Expected dividend yield	—	—	—
Risk-free interest rate	2.3%	2.1%	1.0%

As of December 31, 2017, unrecognized stock-based compensation expense related to unvested non-employees stock options was approximately $0.4 million, which is expected to be recognized over a weighted-average period of 1.5 years, based on the estimated fair value at December 31, 2017.

RSUs

RSUs are share awards that entitle the holder to receive freely tradable shares of the Company's common stock upon vesting. The fair value of RSUs is based upon the closing sales price of the Company's common stock on the grant date. RSUs granted to employees generally vest over a two to four-year period.

The following table summarizes the RSU activity under the Company's stock plans and related information:

(In thousands, except grant date fair value and years)	Number of Units (in thousands)	Weighted-Average Grant Date Fair Value (in dollars)	Weighted-Average Remaining Contractual Term (in years)
Balance at December 31, 2016	1,049	$ 5.47	1.7
Granted	2,543	2.81	
Vested and released	(307)	6.43	
Forfeited	(770)	3.58	
Balance at December 31, 2017	2,515	$ 3.24	1.6

The weighted-average grant-date fair value of RSUs granted during the years ended December 31, 2017, 2016 and 2015 were $2.81, $4.40 and $13.85, respectively. During the years ended December 31, 2017, 2016 and 2015, total fair value of RSUs vested was $2.0 million, $1.7 million and $1.4 million, respectively. The number of RSUs vested includes shares of common stock that the Company withheld on behalf of employees to satisfy the minimum statutory tax withholding requirements. As of December 31, 2017, there was $6.4 million of unrecognized compensation cost related to unvested RSUs that is expected to be recognized over a weighted-average period of 2.9 years.

ESPP

In July 2014, the Company approved the establishment of the 2014 Employee Stock Purchase Plan (the "ESPP"). The Company reserved 208,833 shares of its common stock for issuance and provided for annual increases in the number of shares available for issuance on the first business day of each fiscal year, beginning in 2015, equal to the lesser of one percent (1%) of the number of shares of the Company's common stock outstanding as of such date or a number of shares as determined by the Company's board of directors. During the years ended December 31, 2017, 74,642 shares were issued under the ESPP. As of December 31, 2017, a total of 962,095 shares of common stock were available for future issuance under the ESPP. As of December 31, 2017, unrecognized compensation cost related to the ESPP was immaterial.

Stock-Based Compensation Recognized in the Consolidated Statement of Operations and Comprehensive Loss

The following table presents, by operating expense, the Company's stock-based compensation expense:

	Years ended December 31,		
	2017	2016	2015
	(In thousands)		
Research and development	$ 5,253	$ 6,616	$ 4,009
General and administrative	3,470	4,800	6,447
Restructuring charges	—	—	1,049
Total share-based compensation expense	$ 8,723	$ 11,416	$ 11,505

During the year ended December 31, 2016, stock-based compensation expense included one-time charges of $1.5 million, which was recorded in general and administrative expense, and $1.4 million, which was recorded in research and development expense, related to stock award modifications in connection with the separation agreements for four of Company's executive officers.

During the year ended December 31, 2015, the Company recorded a one-time stock-based compensation expense of $2.4 million related to the cancellation of unvested stock options in connection with the separation agreement for one of the Company's executive officers.

14. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Code. The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. The amount of contributions that the Company made to the 401(k) Plan during the year ended December 31, 2017, 2016 and 2015 was $0.3 million, $0.3 million and $0.1 million, respectively

15. Income Taxes

The Company recorded $0.8 million income tax benefit related to the change in the deferred tax liabilities balance due to intangible assets impairment recognized in the fourth quarter of 2016 and no income tax benefit or expense were recorded for the years ending December 31, 2017 and 2015.

The following table presents domestic and foreign components of loss before provision for income taxes:

	Years ended December 31,		
	2017	2016	2015
	(In thousands)		
U.S.	$ (36,923)	$ (96,498)	$ (47,235)
Foreign	(19,224)	(18,024)	(218)
Loss before income taxes	$ (56,147)	$ (114,522)	$ (47,453)

A reconciliation of income tax expense computed at the statutory federal income tax rate of 34% to income taxes as reflected in the financial statements is as follows:

	Years ended December 31,		
	2017	2016	2015
	(In thousands)		
Federal income tax expense at statutory rate	$ (19,090)	$ (38,938)	$ (16,134)
Non-deductible foreign research expenses	19	21	45
Stock-based compensation	(76)	1,356	1,418
Non-deductible expenses	61	985	295
Goodwill impairment	—	16,834	—
Research and development tax credits	(507)	(326)	(910)
Change in valuation allowance	7,935	16,062	15,277
Foreign rate differential	1,495	3,231	9
Rate change	10,163	—	—
Total tax benefit	$ —	$ (775)	$ —

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The following table presents significant components of the Company's deferred tax assets:

	As of December 31,		
	2017	2016	2015
	(In thousands)		
Deferred tax assets:			
Net operating loss carryforwards	$ 27,142	$ 15,785	$ 19,889
Accruals, reserve and other	2,586	3,071	2,681
Stock-based compensation	3,623	3,848	4,328
Tax credit carryforwards	1,774	574	1,945
Property and equipment	274	54	—
Intangibles	64	68	45
Total deferred tax assets before valuation allowance	35,463	23,400	28,888
Valuation allowance	(35,463)	(23,400)	(28,839)
Total deferred tax assets	—	—	49
Deferred tax liabilities:			
Property and equipment	—	—	(49)
IPR&D	(1,250)	(1,250)	—
Total deferred tax liabilities	$ (1,250)	$ —	$ (49)
Net deferred tax assets	$ —	$ —	$ —

On December 22, 2017, the U.S. government enacted comprehensive tax legislation, commonly known as the Tax Cuts and Jobs Act of 2017 (the "Act"), which significantly reforms the Internal Revenue Code of 1986, as amended. The Act contains broad and complex changes to corporate taxation, including in part reduction of the U.S. federal corporate tax rate from 35% to 21%, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously considered permanently reinvested, and creates new taxes on certain foreign sourced earnings.

As of December 31, 2017, the Company was able to determine a reasonable estimate, namely the one-time transition tax and the remeasurement of deferred tax at the new tax rate. The Company did not recognize any provisional tax expense due to its significant operating losses. The effect on the Company's deferred tax balance due to the change of net tax rate was $10.2 million and was fully offset by its valuation allowance, therefore, there was no net effect to the Company's effective tax rate for the year ended December 31, 2017.

The one-time transition tax is based on the Company's post-1986 foreign earnings and profits which the Company had previously excluded from U.S. income taxes due to its position that it would permanently reinvest its future earnings. The one-time transition tax is applied at a 15.5% tax rate on cash assets and an 8% tax rate for other specified assets. Since the Company's foreign operations incurred aggregated losses, the Company did not record provisional amount for its one-time transition tax liability for its foreign subsidiaries due to overall cumulative foreign losses.

Additionally, the SEC staff has issued SAB 118, which allows the Company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date. On December 22, 2017, Staff Accounting Bulletin No. 118 ("SAB 118") was issued to address the application of U.S. GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Act. Because the Company is still in the process of analyzing certain provisions of the Act including the application of new executive compensation limitation provisions under Internal Revenue Section 162(m) in accordance with SAB 118, the Company determined that the adjustment to its deferred taxes was a provisional amount and a reasonable estimate at December 31, 2017.

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2017, 2016 and 2015. The valuation allowance increased approximately $12.0 million during the years ended December 31, 2017 and decreased approximately $5.3 million during the year ended December 31, 2016.

As of December 31, 2017, the Company had U.S. federal net operating losses ("NOLs") carryforwards of approximately $53.2 million to offset future federal income. NOLs expire at various years beginning with 2036. As of December 31, 2017, the Company also had U.S. state NOL carryforwards of approximately $37.8 million to offset future state income. U.S. State NOLs expire at various years beginning with 2036. At December 31, 2017, the Company also had approximately $44.1 million of foreign net operating loss carryforwards which may be available to offset future foreign income; these carryforwards do not expire.

As of December 31, 2017, the Company had federal research and development tax credit carryforwards of approximately $0.8 million available to reduce future tax liabilities which expire at various years beginning with 2036. As of December 31, 2017, the Company had state credit carryforwards of approximately $1.0 million available to reduce future tax liabilities which do not expire.

Under Section 382 of the Internal Revenue Code of 1986, as amended (Code), the Company's ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if the Company experiences an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. The Company believes that it has experienced ownership changes under Section 382, which will result in limitations in the Company's ability to utilize net operating losses and credits. As a result, the amount of the NOLs and research and credit carryforwards presented in the Company's consolidated financial statements are limited and will expire unutilized, and the Company removed a significant amount of NOLs and credits from its deferred taxes.

The Company files income tax returns in the U.S., and state and foreign jurisdictions. The federal, state and foreign income tax returns are open under the statute of limitations subject to tax examinations for the tax years ended December 31, 2012 through December 31, 2017. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service, state or foreign tax authorities to the extent utilized in a future period.

The Company has total unrecognized tax benefits as of December 31, 2017, 2016 and 2015 of approximately $2.7 million, $2.1 million and $1.6 million, respectively. No amount of the unrecognized tax benefits, if recognized, would reduce the Company's annual effective tax rate because the benefits are in the form of deferred tax assets for which a full valuation allowance has been recorded. The Company does not anticipate a significant change to its unrecognized tax benefits over the next twelve months. A reconciliation of the unrecognized tax benefits is as follows:

	Years ended December 31,		
	2017	2016	2015
	(In thousands)		
Unrecognized tax benefits as of the beginning of the year	$ 2,157	$ 1,568	$ 471
Increase (decrease) related to prior year tax provisions	—	—	172
Increase related to current year tax provisions	588	589	925
Unrecognized tax benefits as of the end of the year	$ 2,745	$ 2,157	$ 1,568

The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2017 and 2016, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive loss. There are no ongoing examinations by taxing authorities at this time.

16. Net Loss per Share

The following common stock equivalents outstanding at the end of the periods presented were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	As of December 31,		
	2017	2016	2015
	(In thousands)		
Stock options	6,695	7,449	5,494
Restricted stock units	2,515	1,049	632
ESPP	71	47	42
Warrants to purchase common stock	90	50	40
	9,371	8,595	6,208

17. Subsequent Events

Editas Agreement

On January 25, 2018, the Company and Editas extended the research collaboration, option and license agreement. In consideration for extending the agreement, Editas made a one-time payment, non-refundable cash payment of $0.5 million to the Company in February 2018.

Under the terms of the agreement, as amended, Editas may exercise the option with respect to a designated initial indication until September 30, 2018. With respect to the four other indications, Editas may exercise the option until the fourth anniversary of the effective date, provided that the option will expire on the third anniversary of the effective date if Editas has not exercised the option with respect to the initial indication or any other indication by such date. Upon Editas' timely exercise of the option with respect to the designated initial indication, Editas will pay the Company a $1.3 million fee. For the first additional indication for which Editas timely exercises its option, Editas will pay the Company a $1.5 million fee. Upon each subsequent exercise of the option, Editas will pay the Company a $1.0 million fee per indication.

Follow-on Offerings of Common Stock

In January 2018, the Company issued and sold a total of 1,419,893 shares of its common stock at market prices under the 2017 stock offering agreement and raised total net proceeds of approximately $5.7 million, net of issuance costs.

In February 2018, the Company completed an underwritten public offering for the sale of 10,222,235 shares of its common stock and raised total net proceeds of approximately $64.3 million, after discounts and other issuance costs.

18. Selected Quarterly Financial Information (Unaudited)

The Company's quarterly consolidated results of operations are shown below:

Quarterly Results of Operations	Three Months Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
	(In thousands, except per share amounts)			
Revenue	$ 462	$ 463	$ 463	$ 461
Total operating expenses (1)	(17,050)	(12,556)	(15,034)	(16,056)
Net loss	(16,099)	(11,430)	(13,829)	(14,789)
Basic and diluted net loss per share	(0.38)	(0.27)	(0.32)	(0.32)

Quarterly Results of Operations	Three Months Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
	(In thousands, except per share amounts)			
Revenue	$ 265	$ 307	$ 395	$ 488
Total operating expenses (2)(3)(4)	(15,773)	(62,189)	(14,902)	(23,875)
Net loss	(15,392)	(61,660)	(14,301)	(22,394)
Basic and diluted net loss per share	(0.57)	(1.76)	(0.35)	(0.54)

(1) During the year ended December 31, 2017, the Company recorded a total of $2.0 million of estimated costs associated with the termination of MSA with Cornell University (see Note 7). During the three months ended March 31, 2017, the Company recorded a total of $2.3 million of these estimated costs, which was subsequently adjusted by $0.3 million during the three months ended June 30, 2017.

(2) During the year ended December 31, 2016, the Company performed a two-step goodwill impairment analysis and recorded $49.1 million and $0.4 million of goodwill impairment charge, respectively, during the three months ended June and September, 2016.

(3) During the three months ended December 31, 2016, the Company performed its annual assessment of its intangible assets, ADVM-043 and ADVM-053, and recorded a total of $11.2 million of impairment charge related to its intangible assets.

(4) During the three months ended March 31, 2016, two officers of the company resigned and the Company recorded $2.2 million of one-time stock-based compensation charge related to the accelerated vesting of their stock-based awards.

Basic and diluted net loss per share is computed independently for each of the quarters presented. Therefore, the sum of quarterly basic and diluted per share amounts may not equal annual basic and diluted net loss per share amounts.

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

Management, including our Principal Executive Officer and Principal Financial Officer, evaluated the effectiveness of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of December 31, 2017. The evaluation of our disclosure controls and procedures included a review of our processes and implementation and the effect on the information generated for use in this Annual Report on Form 10-K. In the course of this evaluation, we sought to identify any material weaknesses in our disclosure controls and procedures to determine whether we had identified any acts of fraud involving personnel who have a significant role in our disclosure controls and procedures, and to confirm that necessary corrective action, including process improvements, was taken. This type of evaluation is done quarterly so that our conclusions concerning the effectiveness of these controls can be reported in our periodic reports filed with the SEC. The overall goals of these evaluation activities are to monitor our disclosure controls and procedures and to make modifications as necessary. We intend to maintain these disclosure controls and procedures, modifying them as circumstances warrant.

Based on that evaluation, the Principal Executive Officer and Principal Financial Officer concluded that as of December 31, 2017, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is (i) recorded, processed, summarized and reported as and when required and (ii) accumulated and communicated to our management, including the Principal Executive Officer and Principal Financial Officer, as appropriate to allow timely discussion regarding required disclosure.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles.

Management assessed our internal control over financial reporting as of December 31, 2017, the end of our fiscal year. Management based its assessment on criteria established in "Internal Control—Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Management's assessment included evaluation of such elements as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies, and our overall control environment. This assessment is supported by testing and monitoring performed by our internal accounting and finance organization.

Based on our assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2017. The results of management's assessment were reviewed with the Audit Committee.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the year ended December 31, 2017 that have materially affected or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Controls and Procedures

Our management, including the Principal Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures and our internal controls will prevent all error and all fraud. A control system, no matter how well designed and operated, can only provide reasonable assurances that the objectives of the control system are met. The design of a control system reflects resource constraints; the benefits of controls must be considered relative to their costs. Because there are inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been or will be detected. As these inherent limitations are known features of the financial reporting process, it is possible to design into the process safeguards to reduce, though not eliminate, these risks. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns occur because of simple error or mistake. Controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls is based in part upon certain assumptions about the likelihood of future events. While our disclosure controls and procedures are designed to provide reasonable assurance of achieving their objectives, there can be no assurance that any design will succeed in achieving its stated goals under all future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with the policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

We intend to review and evaluate the design and effectiveness of our disclosure controls and procedures on an ongoing basis and to improve our controls and procedures over time and to correct any deficiencies that we may discover in the future. While our Principal Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2017, the design of our disclosure controls and procedures, as defined in Rule 13a-15(e) under the Exchange Act, was effective, future events affecting our business may cause us to significantly modify our disclosure controls and procedures.

Item 9B. Other Information.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with our 2018 Annual Meeting of Stockholders (the "Proxy Statement"), which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2017, under the headings "Executive Officers," "Election of Directors," "Corporate Governance," and " Section 16(a) Beneficial Ownership Reporting Compliance," and is incorporated herein by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the Corporate Governance section of our website, which is located at www.adverum.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation.

The information required by this item will be contained in the Proxy Statement under the headings "Executive Compensation" and "Non-Employee Director Compensation," and is incorporated herein by reference.

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

The information required by this item will be contained in the Proxy Statement under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information," and is incorporated herein by reference.

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

The information required by this item will be contained in the Proxy Statement under the headings "Certain Relationships and Related Party Transactions" and "Corporate Governance," and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

The information required by this item will be contained in the Proxy Statement under the heading "Ratification of Selection of Independent Registered Public Accounting Firm" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The financial statements schedules and exhibits filed as part of this Annual Report on Form 10-K are as follows:

See Index to Consolidated Financial Statements in Item 8 of this Annual Report on Form 10-K. No financial statement schedules are provided because the information called for is not required or is shown in the consolidated financial statements or related notes.

(b) The following exhibits are included herein or incorporated by reference:

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
2.1	Acquisition Agreement, dated as of January 29, 2016, by and among Avalanche Biotechnologies, Inc., Annapurna Therapeutics SAS, the Contributors identified therein, and Shareholder Representative Services LLC as the Contributors' Representative.	001-36579	8-K	February 1, 2016	2.1	
2.2	Amendment No. 1 to the Acquisition Agreement, dated as of April 6, 2016.	001-36579	8-K	April 7, 2016	2.1	
3.1	Amended and Restated Certificate of Incorporation.	001-36579	10-K	March 9, 2017	3.1	
3.2	Amended and Restated Bylaws.	001-36579	8-K	May 12, 2016	3.2	
4.1	Reference is made to Exhibits 3.1 through 3.2.					
4.2	Form of Common Stock Certificate.	333-197133	S-1/A	July 25, 2014	4.1	
4.3	Amended and Restated Investor Rights Agreement, dated as of May 11, 2016, by and between Avalanche Biotechnologies, Inc. and certain of its stockholders.	001-36579	8-K	May 12, 2016	4.1	
10.1†	Exclusive License for Use of Recombinant Gene Delivery Vectors for Treating or Preventing Diseases of the Eye, dated as of May 27, 2010, by and between Avalanche Biotechnologies, Inc. and The Regents of the University of California.	333-197133	S-1/A	July 29, 2014	10.1	
10.2†	Research Collaboration and License Agreement, dated as of May 1, 2014, by and between Avalanche Biotechnologies, Inc. and Regeneron Pharmaceuticals, Inc.	333-197133	S-1/A	July 29, 2014	10.3	
10.3†	Amended and Restated Master Service Agreement by and between Annapurna Therapeutics SAS and Cornell University, effective July 15, 2014.	001-36579	10-Q	August 9, 2016	10.3	
10.4†	A1AT Deficiency License Agreement between Annapurna Therapeutics Limited and Cornell University, dated December 15, 2015.	001-36579	10-Q	August 9, 2016	10.4	
10.5†	HAE License Agreement between Annapurna Therapeutics Limited and Cornell University, dated December 15, 2015.	001-36579	10-Q	August 9, 2016	10.5	
10.6†	Allergy License Agreement between Annapurna Therapeutics Limited and Cornell University, dated December 15, 2015.	001-36579	10-Q	August 9, 2016	10.6	
10.7†	License Agreement between AAVLife and Inserm Transfert, dated July 4, 2014.	001-36579	10-Q	August 9, 2016	10.9	
10.8†	Amendment No. 1 to License Agreement between AAVLife and Inserm Transfert, dated October 5, 2015.	001-36579	10-Q	August 9, 2016	10.10	
10.9†	Collaboration, Option and License Agreement with Editas Medicine, Inc., dated August 8, 2016.	001-36579	10-Q	November 8, 2016	10.1	
10.10†	Amendment to Collaboration, Option and License Agreement with Editas Medicine, Inc., dated January 25, 2018.					X
10.11(#)	Avalanche Biotechnologies, Inc. Amended and Restated 2006 Equity Incentive Plan.	333-197133	S-1	June 30, 2014	10.4	

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
10.12(#)	Form of Stock Option Grant Notice and Stock Option Agreement under the Amended and Restated 2006 Equity Incentive Plan.	333-197133	S-1/A	July 25, 2014	10.16	
10.13(#)	Adverum Biotechnologies, Inc. 2014 Equity Incentive Award Plan.					X
10.14(#)	Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan.					X
10.15(#)	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2014 Equity Incentive Award Plan.	333-197133	S-1/A	July 25, 2014	10.18	
10.16(#)	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2014 Equity Incentive Award Plan.					X
10.17(#)	Adverum Biotechnologies, Inc. 2014 Employee Stock Purchase Plan.					X
10.18(#)	Letter Agreement, dated as of June 3, 2013, by and between Avalanche Biotechnologies, Inc. and Mehdi Gasmi.	333-197133	S-1	June 30, 2014	10.10	
10.19(#)	Letter Agreement, dated as of June 13, 2014, by and between Avalanche Biotechnologies, Inc. and Samuel Barone.	333-197133	S-1	December 18, 2014	10.15	
10.20(#)	Separation Agreement, dated September 1, 2017, between Samuel B. Barone, M.D. and Adverum Biotechnologies, Inc.	001-36579	8-K	September 1, 2017	10.1	
10.21(#)	Special Bonus Letter, dated July 23, 2015, for Mehdi Gasmi, Ph.D.	001-36579	8-K	July 23, 2015	10.3	
10.22(#)	Letter Agreement, dated as of August 11, 2015, by and between Avalanche Biotechnologies, Inc. and Mehdi Gasmi, Ph.D.	001-36579	10-Q	August 13, 2015	10.5	
10.23(#)	Offer Letter, dated November 19, 2015, by and between Avalanche Biotechnologies, Inc. and Paul Cleveland.	001-36579	8-K	November 20, 2015	10.1	
10.24(#)	Offer Letter, dated January 29, 2016, by and between Avalanche Biotechnologies, Inc. and Amber Salzman.	001-36579	8-K	February 1, 2016	10.2	
10.25(#)	Change in Control and Severance Agreement, dated January 29, 2016, by and between Amber Salzman and Avalanche Biotechnologies, Inc.	001-36579	8-K	February 1, 2016	10.3	
10.26(#)	Offer Letter, dated June 10, 2016, by and between Adverum Biotechnologies, Inc. and Leone Patterson	001-36579	8-K	June 13, 2016	10.1	
10.27(#)	Amendment to Offer Letter, dated November 2, 2016, by and between Adverum Biotechnologies, Inc. and Amber Salzman.	001-36579	10-K	March 9, 2017	10.39	
10.28(#)	Amendment to Offer Letter, dated November 2, 2016, by and between Adverum Biotechnologies, Inc. and Paul Cleveland.	001-36579	10-K	March 9, 2017	10.40	
10.29(#)	Offer Letter, dated June 15, 2017, by and between Adverum Biotechnologies, Inc. and Athena Countouriotis, M.D.	001-36579	8-K	June 20, 2017	10.1	

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
10.30(#)	Offer Letter, dated May 4, 2015, by and between Avalanche Biotechnologies, Inc. and Jennifer Cheng, Ph.D.					X
10.31	Lease Agreement, dated as of December 20, 2013, by and between Avalanche Biotechnologies, Inc. and O'Brien Drive Portfolio, LLC.		S-1	June 30, 2014	10.11	
10.32	First Amendment to Lease, dated August 1, 2014, by and between O'Brien Drive Portfolio, LLC and Avalanche Biotechnologies, Inc.	001-36579	8-K	September 12, 2014	10.1	
10.33	Second Amendment to Lease, dated October 30, 2014, by and between O'Brien Drive Portfolio, LLC and Avalanche Biotechnologies, Inc.	001-36579	8-K	November 4, 2014	10.1	
10.34(#)	Form of Indemnification Agreement for directors and executive officers.	333-197133	S-1/A	July 18, 2014	10.12	
10.35(#)	2012 Change in Control Benefit Plan.	333-197133	S-1/A	July 18, 2014	10.13	
10.36(#)	Form of Change in Control Severance Agreement for executive officers other than the chief executive officer.					X
10.37(#)	Form of Amendment to the Change in Control and Severance Agreement for Mehdi Gasmi.	001-36579	10-Q	August 13, 2015	10.1	
10.38(#)	Form of Inducement Stock Option Agreement.	001-36579	8-K	November 20, 2015	10.3	
10.39(#)	2017 Inducement Plan.	333-220894	S-8	October 11, 2017	99.1	
10.40(#)	Form of Stock Option Grant Notice and Option Agreement under the 2017 Inducement Plan.	333-220894	S-8	October 11, 2017	99.2	
10.41(#)	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2017 Inducement Plan.	333-220894	S-8	October 11, 2017	99.3	
10.42	Sales Agreement, dated as of August 10, 2017, by and between the Adverum Biotechnologies, Inc. and Cowen and Company, LLC.	333-19890	S-3	August 10, 2017	1.2	
10.43	Release Agreement, dated as of October 3, 2017, by and between the Company and Steven Schwartz, M.D.					X
21.1	List of Subsidiaries.					X
23.1	Consent of Independent Registered Public Accounting Firm.					X
24.1	Power of Attorney (included on signature page hereto)					X
31.1	Certification of Principal Executive Officer, as required by Rule 13a-14(a) or Rule 15d-14(a).					X
31.2	Certification of Chief Financial Officer, as required by Rule 13a-14(a) or Rule 15d-14(a).					X
32.1	Certification pursuant to 18 U.S.C. section 1350, as adopted pursuant to section 906 of the Sarbanes-Oxley Act of 2002.					X

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
101.SCH	XBRL Taxonomy Extension Schema Document.					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.					X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.					X

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

# Indicates management contract or compensatory plan.

* The certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the SEC and is not to be incorporated by reference into any filing of Adverum Biotechnologies, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

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

Date: March 6, 2018

ADVERUM BIOTECHNOLOGIES, INC.

By: /s/ Amber Salzman
Amber Salzman
President and Chief Executive Officer

Power of Attorney

Each person whose individual signature appears below hereby authorizes and appoints Amber Salzman and Leone Patterson, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this annual report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this annual report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Amber Salzman Amber Salzman	President and Chief Executive Officer *(Principal Executive Officer)*	March 6, 2018
/s/Leone Patterson Leone Patterson	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 6, 2018
/s/ Paul B. Cleveland Paul B. Cleveland	Chairman of the Board	March 6, 2018
/s/ Mitchell H. Finer Mitchell H. Finer, Ph.D.	Director	March 6, 2018
/s/ Thomas F. Woiwode Thomas F. Woiwode, Ph.D.	Director	March 6, 2018
/s/ Eric G. Carter Eric G. Carter, M.D., Ph.D.	Director	March 6, 2018
/s/ Patrick Machado Patrick Machado	Director	March 6, 2018
/s/ Richard N. Spivey Richard N. Spivey, Pharm. D.	Director	March 6, 2018

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 10.10

AMENDMENT TO COLLABORATION, OPTION AND LICENSE AGREEMENT

This Amendment ("**Amendment**") is entered into as of January 25, 2018 (the "**Amendment Effective Date**"), by and between **Adverum Biotechnologies, Inc.**, a Delaware corporation having an address at 1035 O'Brien Drive, Menlo Park, CA 94025 ("**Adverum**"), and **Editas Medicine, Inc.**, a Delaware corporation having an address at 11 Hurley St., Cambridge, MA 02141 ("**Editas**") and amends that certain Collaboration, Option and License Agreement, dated August 8, 2016, by and between Adverum and Editas (the "**Agreement**"). Adverum and Editas may be referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

Whereas, Adverum and Editas are parties to the Agreement;

Whereas, the Parties desire to amend the Agreement as set forth herein.

Now, Therefore, in consideration of the mutual covenants and agreements herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties agree as follows.

1. Section 1.74 of the Agreement is hereby deleted in its entirety and replaced with the following:

> **1.74** "**Research Period**" shall mean the period commencing on the Effective Date and ending on the earlier of (i) completion of all research contemplated by the Research Plan (as may be amended from time to time by mutual agreement of the Parties) and (ii) September 30, 2018.

2. The first sentence of Section 3.2 of the Agreement is hereby deleted in its entirety and replaced with the following:

> "Editas may elect, in its sole discretion, to exercise the Option with respect to the Initial Indication by providing written notice to Adverum at any time by September 30, 2018 (the "**Initial Option Exercise Period**")."

3. The first sentence of Section 3.3 of the Agreement is hereby deleted in its entirety and replaced with the following:

> "Whether or not Editas exercises the Option with respect to the Initial Indication within the Initial Option Exercise Period, Editas shall have the right to elect, in its sole discretion, to exercise the Option with respect to one or more (and up to all) of the Additional Indications by providing written notice to Adverum, provided that Editas shall exercise all such Options within the four years following the Effective Date (the "**Additional Indication Option Exercise Period**"), provided, that Editas has either made the Initial Option Exercise or has made an option exercise pursuant to this Section 3.3 during the three (3) year period following the Effective Date."

4. Section 6.2 of the Agreement is hereby deleted in its entirety and replaced with the following:

> "**6.2 (a) Option Extension Fee.** In consideration for the parties entering into that certain Amendment to Collaboration, Option and License Agreement, by and between the parties, dated January 25, 2018 (the "**Amendment**"), Editas shall make a one-time, non-refundable, noncreditable payment to Adverum of five hundred thousand dollars ($500,000.00) within [*] days after the effective date of the Amendment, provided, that Adverum has provided an invoice for such payment to accounts.payable@editasmed.com.
>
> **6.2 (b) Option Exercise Fee.** Editas shall make a one-time, nonrefundable, non-creditable payment to Adverum of one million three hundred thousand dollars ($1,300,000) if and when Editas decides, in its sole discretion, to timely make the Option Exercise. Additionally, for the first Additional Indication for which Editas timely exercises its Option, as determined in Editas' sole discretion, Editas shall make a one-time, nonrefundable, non-creditable payment to Adverum of one million five hundred thousand dollars ($1,500,000.00) for such Additional Indication for which it exercises its Option to take a license under Section 3.4(a). Editas shall make a one-time, non-refundable, non-creditable payment to Adverum of one million dollars ($1,000,000.00) for each Additional Indication (other than the first Additional Indication for which Editas may exercise the Option as contemplated by the prior sentence) for which it exercises its Option, as determined in Editas' sole discretion, for such Additional Indication for which it exercises its Option to take a license under Section 3.4(a). Payment of the sums associated with each Option exercise set forth in this Section 6.2(b) shall be made within [*] business days after the applicable Option Exercise Date."

5. The Research Plan set forth in the Agreement shall be amended and replaced in its entirety with the Research Plan attached hereto as **Schedule A**.

6. Each Party hereby provides written notice to the other Party that its respective JRC representatives are updated and revised as follows:

   Adverurn JRC representatives:
   a. Mehdi Gasmi, Chief Science and Technology Officer
   b. Angelica Philips, VP, Preclinical Development
   c. Pallavi Sharma, Scientist, Assay Development

   Editas JRC representatives:
   a. Charlie Albright, Chief Scientific Officer
   b. Peter Baciu, Senior Director, Ocular Diseases
   c. Jonathan McNeill, Senior Manager, Business Development

7. The Parties acknowledge and agree that this Amendment shall not amend or change the fact that five hundred thousand dollars ($500,000) of the payment made by Editas pursuant to Section 6.1 of the Agreement (minus any amounts that Editas has already credited against payments owed pursuant to Section 2.2(c)) is creditable against amounts Editas may owe to Adverum pursuant to Section 2.2(c). The Parties further acknowledge and agree that $37,191.45 of such credit has been utilized as of the Amendment Effective Date resulting in a balance of $462,808.55 creditable against amounts Editas may owe to Adverum pursuant to Section 2.2(c).

8. The Parties acknowledge and agree that notwithstanding anything to the contrary in the Agreement or this Amendment, there shall not be a Non-Adverum Product and no rights are granted under the Agreement or this Amendment with respect to any Non-Adverum Product.

9. Capitalized terms used and not defined herein shall have the meaning ascribed to such terms in the Agreement. All references herein to paragraph or section location shall relate to the corresponding paragraph or section in the Agreement.

10. Except as specifically set forth in this Amendment, the Agreement will continue in full force and effect without change. If there is any conflict between the terms of this Amendment and the Agreement, this Amendment will govern.

11. This Amendment may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument. This Amendment may be executed and delivered electronically or by facsimile and upon such delivery such electronic or facsimile signature will be deemed to have the same effect as if the original signature had been delivered to the other Party.

12. Governing Law. This Amendment shall be governed by and construed in accordance with the laws of the State of Delaware, US, without reference to any rules of conflict of laws.

{Signature Page Follows}

In Witness Whereof, the Parties hereto have caused this Amendment to be executed and entered into by their duly authorized representatives as of the Amendment Effective Date.

Adverum Biotechnologies, Inc.		**Editas Medicine, Inc.**	
By:	/s/ Amber Salzman	By:	/s/ Charlie Albright
Name:	Amber Salzman	Name:	Charlie Albright
Title:	President and CEO	Title:	Chief Scientific Officer

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Schedule A

Research Plan

[*]

(5 pages omitted)

[*] = Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

Exhibit 10.13

ADVERUM BIOTECHNOLOGIES, INC.
2014 EQUITY INCENTIVE AWARD PLAN

ARTICLE 1.
PURPOSE

The purpose of the Adverum Biotechnologies, Inc. 2014 Equity Incentive Award Plan (as it may be amended from time to time, the "Plan") is to promote the success and enhance the value of Adverum Biotechnologies, Inc. (the "Company") by linking the individual interests of the members of the Board, Employees, and Consultants to those of the Company's stockholders and by providing such individuals with an incentive for outstanding performance to generate superior returns to the Company's stockholders. The Plan is further intended to provide flexibility to the Company in its ability to motivate, attract, and retain the services of members of the Board, Employees, and Consultants upon whose judgment, interest, and special effort the successful conduct of the Company's operation is largely dependent.

ARTICLE 2.
DEFINITIONS AND CONSTRUCTION

Wherever the following terms are used in the Plan they shall have the meanings specified below, unless the context clearly indicates otherwise. The singular pronoun shall include the plural where the context so indicates.

2.1 "Administrator" shall mean the entity that conducts the general administration of the Plan as provided in Article 13 hereof. With reference to the duties of the Administrator under the Plan which have been delegated to one or more persons pursuant to Section 13.6 hereof, or as to which the Board has assumed, the term "Administrator" shall refer to such person(s) unless the Committee or the Board has revoked such delegation or the Board has terminated the assumption of such duties.

2.2 "Affiliate" shall mean any Parent or Subsidiary.

2.3 "Applicable Accounting Standards" shall mean Generally Accepted Accounting Principles in the United States, International Financial Reporting Standards or such other accounting principles or standards as may apply to the Company's financial statements under United States federal securities laws from time to time.

2.4 "Applicable Law" shall mean any applicable law, including without limitation, (i) provisions of the Code, the Securities Act, the Exchange Act and any rules or regulations thereunder; (ii) corporate, securities, tax or other laws, statutes, rules, requirements or regulations, whether federal, state, local or foreign; and (iii) rules of any securities exchange or automated quotation system on which the Shares are listed, quoted or traded.

2.5 "Award" shall mean an Option, a Restricted Stock award, a Restricted Stock Unit award, a Performance Award, a Dividend Equivalents award, a Deferred Stock award, a Deferred Stock Unit award, a Stock Payment award or a Stock Appreciation Right, which may be awarded or granted under the Plan (collectively, "Awards").

2.6 "Award Agreement" shall mean any written notice, agreement, terms and conditions, contract or other instrument or document evidencing an Award, including through electronic medium, which shall contain such terms and conditions with respect to an Award as the Administrator shall determine consistent with the Plan.

2.7 "Board" shall mean the Board of Directors of the Company.

2.8 "Cause" shall mean, unless such term or an equivalent term is otherwise defined by the applicable Award Agreement or other written agreement between a Holder and the Company applicable to an Award, the occurrence of any of the following events: (i) conviction of any felony or crime involving moral turpitude or dishonesty; (ii) willful and material breach of the Holder's duties that has not been cured within 30 days after written notice from the Board of Directors; (iii) intentional and material damage to the Company's property; or (iv) material breach of the Proprietary Information and Inventions Agreement executed by the Holder.

2.9 "Change in Control" shall mean the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(a) A transaction or series of transactions (other than an offering of Common Stock to the general public through a registration statement filed with the Securities and Exchange Commission) whereby any "person" or related "group" of "persons" (as such terms are used in Sections 13(d) and 14(d)(2) of the Exchange Act) (other than the Company, any of its subsidiaries, an employee benefit plan maintained by the Company or any of its subsidiaries or a "person" that, prior to such transaction, directly or indirectly controls, is controlled by, or is under common control with, the Company) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of securities of the Company possessing more than 50% of the total combined voting power of the Company's securities outstanding immediately after such acquisition; or

(b) During any period of two consecutive years, individuals who, at the beginning of such period, constitute the Board together with any new Director(s) (other than a Director designated by a person who shall have entered into an agreement with the Company to effect a transaction described in Section 2.9(a) or 2.9(c)) whose election by the Board or nomination for election by the Company's stockholders was approved by a vote of at least two- thirds of the Directors then still in office who either were Directors at the beginning of the two- year period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority thereof; or

(c) The consummation by the Company (whether directly involving the Company or indirectly involving the Company through one or more intermediaries) of (x) a merger, consolidation, reorganization, or business combination or (y) a sale or

other disposition of all or substantially all of the Company's assets in any single transaction or series of related transactions or (z) the acquisition of assets or stock of another entity, in each case other than a transaction:

(i) which results in the Company's voting securities outstanding immediately before the transaction continuing to represent (either by remaining outstanding or by being converted into voting securities of the Company or the person that, as a result of the transaction, controls, directly or indirectly, the Company or owns, directly or indirectly, all or substantially all of the Company's assets or otherwise succeeds to the business of the Company (the Company or such person, the "Successor Entity")) directly or indirectly, at least a majority of the combined voting power of the Successor Entity's outstanding voting securities immediately after the transaction, and

(ii) after which no person or group beneficially owns voting securities representing 50% or more of the combined voting power of the Successor Entity; provided, however, that no person or group shall be treated for purposes of this Section 2.9(c)(ii) as beneficially owning 50% or more of the combined voting power of the Successor Entity solely as a result of the voting power held in the Company prior to the consummation of the transaction; or

(d) The Company's stockholders approve a liquidation or dissolution of the Company.

Notwithstanding the foregoing, if a Change in Control constitutes a payment event with respect to any portion of an Award that provides for the deferral of compensation and is subject to Section 409A of the Code, the transaction or event described in subsection (a), (b), (c) or (d) with respect to such Award (or portion thereof) must also constitute a "change in control event," as defined in Treasury Regulation Section 1.409A-3(i)(5) to the extent required by Section 409A.

The Committee shall have full and final authority, which shall be exercised in its discretion, to determine conclusively whether a Change in Control of the Company has occurred pursuant to the above definition, and the date of the occurrence of such Change in Control and any incidental matters relating thereto; provided that any exercise of authority is in conjunction with a determination of whether a Change in Control is a "change in control event" as defined in Treasury Regulation Section 1.409A-3(i)(5) shall be consistent with such regulation.

2.10 "Code" shall mean the Internal Revenue Code of 1986, as amended from time to time, together with the regulations and official guidance promulgated thereunder, whether issued prior or subsequent to the grant of any Award.

2.11 "Committee" shall mean the Compensation Committee of the Board, a subcommittee of the Compensation Committee of the Board or another committee or subcommittee of the Board, appointed as provided in Section 13.1 hereof.

2.12 "Common Stock" shall mean the common stock of the Company, par value $0.0001 per share.

2.13 "Company" shall have the meaning set forth in Article 1 hereof.

2.14 "Consultant" shall mean any consultant or advisor engaged to provide services to the Company or any Affiliate who qualifies as a consultant or advisor under the applicable rules of the Securities and Exchange Commission for registration of shares on a Form S-8 Registration Statement or any successor Form thereto or, prior to the Public Trading Date, under Rule 701 of the Securities Act.

2.15 "Covered Employee" shall mean any Employee who is, or could be, a "covered employee" within the meaning of Section 162(m) of the Code.

2.16 "Deferred Stock" shall mean a right to receive Shares awarded under Section 10.4 hereof.

2.17 "Deferred Stock Unit" shall mean a right to receive Shares awarded under Section 10.5 hereof.

2.18 "Director" shall mean a member of the Board, as constituted from time to time.

2.19 "Dividend Equivalent" shall mean a right to receive the equivalent value (in cash or Shares) of dividends paid on Shares, awarded under Section 10.2 hereof.

2.20 "DRO" shall mean a "domestic relations order" as defined by the Code or Title I of the Employee Retirement Income Security Act of 1974, as amended from time to time, or the rules thereunder.

2.21 "Effective Date" shall mean immediately prior to the time at which the Company registration statement relating to its initial public offering becomes effective, provided that the Board has adopted the Plan prior to or on such date, subject to approval of the Plan by the Company's stockholders.

2.22 "Eligible Individual" shall mean any person who is an Employee, a Consultant or a Non-Employee Director, as determined by the Administrator.

2.23 "Employee" shall mean any officer or other employee (as determined in accordance with Section 3401(c) of the Code and the Treasury Regulations thereunder) of the Company or any Affiliate.

2.24 "Equity Restructuring" shall mean a nonreciprocal transaction between the Company and its stockholders, such as a stock dividend, stock split, spin-off, rights offering or recapitalization through a large, nonrecurring cash dividend, that affects the number or kind of Shares (or other securities of the Company) or the share price of Common Stock (or other securities) and causes a change in the per share value of the Common Stock underlying outstanding stock-based Awards.

2.25 "Exchange Act" shall mean the Securities Exchange Act of 1934, as amended from time to time.

2.26 "Fair Market Value" shall mean, as of any given date, the value of a Share determined as follows:

(a) If the Common Stock is (i) listed on any established securities exchange (such as the New York Stock Exchange, the NASDAQ Global Market and the NASDAQ Global Select Market), (ii) listed on any national market system or (iii) listed, quoted or traded on any automated quotation system, its Fair Market Value shall be the closing sales price for a Share as quoted on such exchange or system for such date or, if there is no closing sales price for a Share on the date in question, the closing sales price for a Share on the last preceding date for which such quotation exists, as reported in The Wall Street Journal or such other source as the Administrator deems reliable;

(b) If the Common Stock is not listed on an established securities exchange, national market system or automated quotation system, but the Common Stock is regularly quoted by a recognized securities dealer, its Fair Market Value shall be the mean of the high bid and low asked prices for such date or, if there are no high bid and low asked prices for a Share on such date, the high bid and low asked prices for a Share on the last preceding date for which such information exists, as reported in The Wall Street Journal or such other source as the Administrator deems reliable; or

(c) If the Common Stock is neither listed on an established securities exchange, national market system or automated quotation system nor regularly quoted by a recognized securities dealer, its Fair Market Value shall be established by the Administrator in good faith.

Notwithstanding the foregoing, with respect to any Award granted after the effectiveness of the Company's registration statement relating to its initial public offering and prior to the Public Trading Date, the Fair Market Value shall mean the initial public offering price of a Share as set forth in the Company's final prospectus relating to its initial public offering filed with the Securities and Exchange Commission.

2.27 "Good Reason" shall mean, unless such term or an equivalent term is otherwise defined by the applicable Award Agreement or other written agreement between a Holder and the Company applicable to an Award, with respect to any particular Holder, the Holder's resignation from all positions he or she then-holds with the Company if (A) without Holder's written consent (I) there is a material reduction of the Holder's base salary; *provided*, *however*, that a material reduction in the Holder's base salary pursuant to a salary reduction program affecting all or substantially all of the employees of the Company and that does not adversely affect Holder to a greater extent than other similarly situated employees shall not constitute Good Reason; or (II) the Holder is required to relocate his or her primary work location to a facility or location that would increase the Holder's one way commute distance by more than fifty (50) miles from the Holder's primary work location as of immediately prior to such change, (B) the Holder provides written notice outlining such conditions, acts or omissions to the Company's General Counsel within thirty (30) days immediately following such material change or reduction, (C) such material change or reduction is not remedied by the Company within thirty (30) days following the Company's receipt of such written notice and (D) the Holder's resignation is effective not later than thirty (30) days after the expiration of such thirty (30) day cure period.

2.28 "Greater Than 10% Stockholder" shall mean an individual then owning (within the meaning of Section 424(d) of the Code) more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or any "parent corporation" or "subsidiary corporation" (as defined in Sections 424(e) and 424(f) of the Code, respectively).

2.29 "Holder" shall mean a person who has been granted an Award.

2.30 "Incentive Stock Option" shall mean an Option that is intended to qualify as an incentive stock option and conforms to the applicable provisions of Section 422 of the Code.

2.31 "Non-Employee Director" shall mean a Director of the Company who is not an Employee.

2.32 "Non-Employee Director Equity Compensation Policy" shall have the meaning set forth in Section 4.6 hereof.

2.33 "Non-Qualified Stock Option" shall mean an Option that is not an Incentive Stock Option or which is designated as an Incentive Stock Option but does not meet the applicable requirements of Section 422 of the Code.

2.34 "Option" shall mean a right to purchase Shares at a specified exercise price, granted under Article 6 hereof. An Option shall be either a Non-Qualified Stock Option or an Incentive Stock Option; provided, however, that Options granted to Non-Employee Directors and Consultants shall only be Non-Qualified Stock Options.

2.35 "Option Term" shall have the meaning set forth in Section 6.4 hereof.

2.36 "Parent" shall mean any entity (other than the Company), whether domestic or foreign, in an unbroken chain of entities ending with the Company if each of the entities other than the Company beneficially owns, at the time of the determination, securities or interests representing more than fifty percent (50%) of the total combined voting power of all classes of securities or interests in one of the other entities in such chain.

2.37 "Performance Award" shall mean a cash bonus award, stock bonus award, performance award or incentive award that is paid in cash, Shares or a combination of both, awarded under Section 10.1 hereof.

2.38 "Performance-Based Compensation" shall mean any compensation that is intended to qualify as "performance-based compensation" as described in Section 162(m)(4)(C) of the Code.

2.39 "Performance Criteria" shall mean the criteria (and adjustments) that the Committee selects for an Award for purposes of establishing the Performance Goal or Performance Goals for a Performance Period, determined as follows:

(a) The Performance Criteria that shall be used to establish Performance Goals are limited to the following: (i) net earnings (either before or after one or more of the following: (A) interest, (B) taxes, (C) depreciation, (D) amortization and (E) non-cash equity-based compensation expense); (ii) gross or net sales or revenue;

(iii) net income (either before or after taxes); (iv) adjusted net income; (v) operating income, earnings or profit (either before or after taxes); (vi) cash flow (including, but not limited to, cash flow return on investments, operating cash flow and free cash flow); (vii) return on assets; (viii) return on capital; (ix) return on stockholders' equity; (x) total stockholder return; (xi) return on sales; (xii) gross or net profit or operating margin; (xiii) costs; (xiv) funds from operations; (xv) expenses; (xvi) working capital; (xvii) earnings per Share; (xviii) adjusted earnings per share; (xix) price per Share; (xx) regulatory body approval for commercialization of a product; (xxi) implementation or completion of critical projects; (xxii) market share; (xxiii) economic value; (xxiv) debt levels or reduction; (xxv) customer retention; (xxvi) sales-related goals; (xxvii) comparisons with other stock market indices; (xxviii) operating efficiency; (xxix) customer satisfaction and/or growth; (xxx) employee satisfaction; (xxxi) research and development achievements; (xxxii) financing and other capital raising transactions; (xxxiii) recruiting and maintaining personnel; and (xxxiv) year-end cash, any of which may be measured either in absolute terms for the Company or any operating unit of the Company or as compared to any incremental increase or decrease or as compared to results of a peer group or to market performance indicators or indices.

(b) The Administrator may, in its sole discretion, provide that one or more objectively determinable adjustments shall be made to one or more of the Performance Goals. Such adjustments may include, but are not limited to, one or more of the following: (i) items related to a change in accounting principle; (ii) items relating to financing activities; (iii) expenses for restructuring or productivity initiatives; (iv) other non-operating items; (v) items related to acquisitions; (vi) items attributable to the business operations of any entity acquired by the Company during the Performance Period; (vii) items related to the sale or disposition of a business or segment of a business; (viii) items related to discontinued operations that do not qualify as a segment of a business under Applicable Accounting Standards; (ix) items attributable to any stock dividend, stock split, combination or exchange of stock occurring during the Performance Period; (x) any other items of significant income or expense which are determined to be appropriate adjustments; (xi) items relating to unusual or extraordinary corporate transactions, events or developments, (xii) items related to amortization of acquired intangible assets; (xiii) items that are outside the scope of the Company's core, on-going business activities; (xiv) items related to acquired in-process research and development; (xv) items relating to changes in tax laws; (xvi) items relating to major licensing or partnership arrangements; (xvii) items relating to asset impairment charges; (xviii) items relating to gains or losses for litigation, arbitration and contractual settlements; or (xix) items relating to any other unusual or nonrecurring events or changes in Applicable Laws, accounting principles or business conditions. For all Awards intended to qualify as Performance-Based Compensation, such determinations shall be made within the time prescribed by, and otherwise in compliance with, Section 162(m) of the Code.

2.40 "Performance Goals" shall mean, with respect to a Performance Period, one or more goals established in writing by the Administrator for the Performance Period based upon one or more Performance Criteria. Depending on the Performance Criteria used to establish such Performance Goals, the Performance Goals may be expressed in terms of overall Company performance or the performance of an Affiliate, a division, business unit or one or more individuals. The achievement of each Performance Goal shall be determined, to the extent applicable, with reference to Applicable Accounting Standards.

2.41 "Performance Period" shall mean one or more periods of time, which may be of varying and overlapping durations, as the Administrator may select, over which the attainment of one or more Performance Goals will be measured for the purpose of determining a Holder's right to, and the payment of, a Performance Award.

2.42 "Performance Stock Unit" shall mean a Performance Award awarded under Section 10.1 hereof which is denominated in units of value including dollar value of shares of Common Stock.

2.43 "Permitted Transferee" shall mean, with respect to a Holder, (a) prior to the Public Trading Date, any "family member" of the Holder, as defined under Rule 701 of the Securities Act and (b) on or after the Public Trading Date, any "family member" of the Holder, as defined under the General Instructions to Form S-8 Registration Statement under the Securities Act or any successor Form thereto, or any other transferee specifically approved by the Administrator, after taking into account Applicable Law.

2.44 "Plan" shall have the meaning set forth in Article 1 hereof.

2.45 "Prior Plan" shall mean the Avalanche Biotechnologies, Inc. Amended and Restated 2006 Equity Incentive Plan, as such plan may be amended from time to time.

2.46 "Program" shall mean any program adopted by the Administrator pursuant to the Plan containing the terms and conditions intended to govern a specified type of Award granted under the Plan and pursuant to which such type of Award may be granted under the Plan.

2.47 "Public Trading Date" shall mean the first date upon which the Common Stock is listed (or approved for listing) upon notice of issuance on any securities exchange or designated (or approved for designation) upon notice of issuance as a national market security on an interdealer quotation system.

2.48 "Restricted Stock" shall mean an award of Shares made under Article 8 hereof that is subject to certain restrictions and may be subject to risk of forfeiture or repurchase.

2.49 "Restricted Stock Unit" shall mean a contractual right awarded under Article 9 hereof to receive in the future a Share or the Fair Market Value of a Share in cash.

2.50 "Securities Act" shall mean the Securities Act of 1933, as amended.

2.51 "Shares" shall mean shares of Common Stock.

2.52 "Share Limit" shall have the meaning set forth in Section 3.1(a) hereof.

2.53 "Stock Appreciation Right" shall mean a stock appreciation right granted under Article 11 hereof.

2.54 "Stock Appreciation Right Term" shall have the meaning set forth in Section 11.4 hereof.

2.55 "Stock Payment" shall mean (a) a payment in the form of Shares, or (b) an option or other right to purchase Shares, as part of a bonus, deferred compensation or other arrangement, awarded under Section 10.3 hereof.

2.56 "Subsidiary" shall mean any entity (other than the Company), whether domestic or foreign, in an unbroken chain of entities beginning with the Company if each of the entities other than the last entity in the unbroken chain beneficially owns, at the time of the determination, securities or interests representing more than fifty percent (50%) of the total combined voting power of all classes of securities or interests in one of the other entities in such chain.

2.57 "Substitute Award" shall mean an Award granted under the Plan upon the assumption of, or in substitution for, outstanding equity awards previously granted by a company or other entity in connection with a corporate transaction, such as a merger, combination, consolidation or acquisition of property or stock; provided, however, that in no event shall the term "Substitute Award" be construed to refer to an award made in connection with the cancellation and repricing of an Option or Stock Appreciation Right.

2.58 "Termination of Service" shall mean:

(a) As to a Consultant, the time when the engagement of a Holder as a Consultant to the Company or an Affiliate is terminated for any reason, with or without cause, including, without limitation, by resignation, discharge, death or retirement, but excluding terminations where the Consultant simultaneously commences or remains in employment or service with the Company or any Affiliate.

(b) As to a Non-Employee Director, the time when a Holder who is a Non- Employee Director ceases to be a Director for any reason, including, without limitation, a termination by resignation, failure to be elected, death or retirement, but excluding terminations where the Holder simultaneously commences or remains in employment or service with the Company or any Affiliate.

(c) As to an Employee, the time when the employee-employer relationship between a Holder and the Company or any Affiliate is terminated for any reason, including, without limitation, a termination by resignation, discharge, death, disability or retirement; but excluding terminations where the Holder simultaneously commences or remains in employment or service with the Company or any Affiliate.

The Administrator, in its sole discretion, shall determine the effect of all matters and questions relating to Terminations of Service, including, without limitation, the question of whether

a Termination of Service resulted from a discharge for cause and all questions of whether particular leaves of absence constitute a Termination of Service; provided, however, that, with respect to Incentive Stock Options, unless the Administrator otherwise provides in the terms of the Program, the Award Agreement or otherwise, a leave of absence, change in status from an employee to an independent contractor or other change in the employee-employer relationship shall constitute a Termination of Service only if, and to the extent that, such leave of absence, change in status or other change interrupts employment for the purposes of Section

422(a)(2) of the Code and the then applicable regulations and revenue rulings under said Section. For purposes of the Plan, a Holder's employee-employer relationship or consultancy relations shall be deemed to be terminated in the event that the Affiliate employing or contracting with such Holder ceases to remain an Affiliate following any merger, sale of stock or other corporate transaction or event (including, without limitation, a spin-off).

ARTICLE 3.

SHARES SUBJECT TO THE PLAN

3.1 Number of Shares.

(a) Subject to Sections 14.1, 14.2 and 3.1(b) hereof, the aggregate number of Shares which may be issued or transferred pursuant to Awards under the Plan shall be equal to the sum of (i) 2,088,332 Shares, (ii) any of the Shares which as of the Effective Date are available for issuance under the Prior Plan, or are subject to awards under the Prior Plan that, on or after the Effective Date, terminate, expire or lapse for any reason without the delivery of Shares to the holder thereof, up to a maximum of 5,384,000 Shares, and (iii) an annual increase on the first day of each year beginning in 2015 and ending in 2024, in each case subject to the approval of the Administrator on or prior to the applicable date, equal to the lesser of (A) four percent (4%) of the Shares outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (B) such smaller number of Shares as determined by the Board (such sum, the "Share Limit"); provided, however, no more than 10,441,663 Shares may be issued upon the exercise of Incentive Stock Options. Notwithstanding the foregoing, Shares added to the Share Limit pursuant to Section 3.1(a)(ii) or Section 3.1(a)(iii) hereof shall be available for issuance as Incentive Stock Options only to the extent that making such Shares available for issuance as Incentive Stock Options would not cause any Incentive Stock Option to cease to qualify as such. Notwithstanding the foregoing, to the extent permitted under Applicable Law, Awards that provide for the delivery of Shares subsequent to the applicable grant date may be granted in excess of the Share Limit if such Awards provide for the forfeiture or cash settlement of such Awards to the extent that insufficient Shares remain under the Share Limit in this Section 3.1 at the time that Shares would otherwise be issued in respect of such Award. As of the Effective Date, no further awards may be granted under the Prior Plan; however, any awards under the Prior Plan that are outstanding as of the Effective Date shall continue to be subject to the terms and conditions of the Prior Plan.

(b) If any Shares subject to an Award are forfeited or expire or such Award is settled for cash (in whole or in part), the Shares subject to such Award shall, to the extent of such forfeiture, expiration or cash settlement, again be available for future grants of Awards under the Plan and shall be added back to the Share Limit. In addition, the following Shares shall be available for future grants of Awards under the Plan and shall be added back to the Share Limit:

(i) Shares tendered by a Holder or withheld by the Company in payment of the exercise price of an Option; (ii) Shares tendered by the Holder or withheld by the Company to satisfy any tax withholding obligation with respect to an Award; and (iii) Shares subject to Stock Appreciation Rights that are not issued in connection with the stock settlement of the Stock Appreciation Rights on exercise thereof. Notwithstanding anything to the contrary contained herein, Shares purchased on the open market with the cash proceeds from the exercise of Options shall not be added back to the Share Limit and shall not be available for future grants of Awards. Any Shares repurchased by the Company under Section 8.4 hereof at the same price paid by the Holder or a lower price so that such Shares are returned to the Company will again be available for Awards. The payment of Dividend Equivalents in cash in conjunction with any outstanding Awards shall not be counted against the Shares available for issuance under the Plan. Notwithstanding the provisions of this Section 3.1(b), no Shares may again be optioned, granted or awarded if such action would cause an Incentive Stock Option to fail to qualify as an incentive stock option under Section 422 of the Code.

(c) Substitute Awards shall not reduce the Shares authorized for grant under the Plan. Additionally, in the event that a company acquired by the Company or any Affiliate or with which the Company or any Affiliate combines has shares available under a pre-existing plan approved by its stockholders and not adopted in contemplation of such acquisition or combination, the shares available for grant pursuant to the terms of such pre-existing plan (as adjusted, to the extent appropriate, using the exchange ratio or other adjustment or valuation ratio or formula used in such acquisition or combination to determine the consideration payable to the holders of common stock of the entities party to such acquisition or combination) may be used for Awards under the Plan and shall not reduce the Shares authorized for grant under the Plan; provided that Awards using such available shares shall not be made after the date awards or grants could have been made under the terms of the pre-existing plan, absent the acquisition or combination, and shall only be made to individuals who were not employed by or providing services to the Company or its Affiliates immediately prior to such acquisition or combination.

3.2 Stock Distributed. Any Shares distributed pursuant to an Award may consist, in whole or in part, of authorized and unissued Common Stock, treasury Common Stock or Common Stock purchased on the open market.

3.3 Limitation on Number of Shares Subject to Awards to Non-Employee Directors. The maximum aggregate value of Awards (with such value determined as of the date of grant under Applicable Accounting Standards) that may be granted to any Non-Employee Director during any calendar year shall be $750,000.

ARTICLE 4.

GRANTING OF AWARDS

4.1 Participation. The Administrator may, from time to time, select from among all Eligible Individuals, those to whom an Award shall be granted and shall determine the nature and amount of each Award, which shall not be inconsistent with the requirements of the Plan. Except as provided in Section 4.6 hereof regarding the grant of Awards pursuant to the Non- Employee Director Equity Compensation Policy, no Eligible Individual shall have any right to be granted an Award pursuant to the Plan.

4.2 Award Agreement. Each Award shall be evidenced by an Award Agreement that sets forth the terms, conditions and limitations for such Award, which may include the term of the Award, the provisions applicable in the event of the Holder's Termination of Service, and the Company's authority to unilaterally or bilaterally amend, modify, suspend, cancel or rescind an Award. Award Agreements evidencing Awards intended to qualify as Performance-Based Compensation shall contain such terms and conditions as may be necessary to meet the applicable provisions of Section 162(m) of the Code. Award Agreements evidencing Incentive Stock Options shall contain such terms and conditions as may be necessary to meet the applicable provisions of Section 422 of the Code.

4.3 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan, the Plan, and any Award granted or awarded to any individual who is then subject to Section 16 of the Exchange Act, shall be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including Rule 16b-3 of the Exchange Act and any amendments thereto) that are requirements for the application of such exemptive rule. To the extent permitted by Applicable Law, the Plan and Awards granted or awarded hereunder shall be deemed amended to the extent necessary to conform to such applicable exemptive rule.

4.4 At-Will Employment; Voluntary Participation. Nothing in the Plan or in any Program or Award Agreement hereunder shall confer upon any Holder any right to continue in the employ of, or as a Director or Consultant for, the Company or any Affiliate, or shall interfere with or restrict in any way the rights of the Company and any Affiliate, which rights are hereby expressly reserved, to discharge any Holder at any time for any reason whatsoever, with or without cause, and with or without notice, or to terminate or change all other terms and conditions of employment or engagement, except to the extent expressly provided otherwise in a written agreement between the Holder and the Company or any Affiliate. Participation by each Holder in the Plan shall be voluntary and nothing in the Plan shall be construed as mandating that any Eligible Individual shall participate in the Plan.

4.5 Foreign Holders. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws in countries other than the United States in which the Company and its Affiliates operate or have Employees, Non-Employee Directors or Consultants, or in order to comply with the requirements of any foreign securities exchange, the Administrator, in its sole discretion, shall have the power and authority to: (a) determine which Affiliates shall be covered by the Plan; (b) determine which Eligible Individuals outside the United States are eligible to participate in the Plan; (c) modify the terms and conditions of any Award granted to Eligible Individuals outside the United States to comply with applicable foreign laws or listing requirements of any such foreign securities exchange; (d) establish subplans and modify exercise procedures and other terms and procedures, to the extent such actions may be necessary or advisable (any such subplans and/or modifications shall be attached to the Plan as appendices); provided, however, that no such subplans and/or modifications shall increase the share limitations contained in Sections 3.1 and 3.3 hereof; and (e) take any action, before or after an Award is made, that it deems advisable to obtain approval or comply with any necessary local governmental regulatory exemptions or approvals or listing requirements of any such foreign securities exchange. Notwithstanding the foregoing, the Administrator may not take any actions hereunder, and no Awards shall be granted, that would violate the Code, the Exchange Act, the Securities Act, any other securities law or governing statute, the rules of the securities exchange or automated quotation system on which the Shares are listed, quoted or traded or any other Applicable Law. For purposes of the Plan, all references to foreign laws, rules, regulations or taxes shall be references to the laws, rules, regulations and taxes of any applicable jurisdiction other than the United States or a political subdivision thereof.

4.6 Non-Employee Director Awards. The Administrator may, in its discretion, provide that Awards granted to Non-Employee Directors shall be granted pursuant to a written non-discretionary formula established by the Administrator (the "Non-Employee Director Equity Compensation Policy"), subject to the limitations of the Plan. The Non-Employee Director Equity Compensation Policy shall set forth the type of Award(s) to be granted to Non- Employee Directors, the number of Shares to be subject to Non-Employee Director Awards, the conditions on which such Awards shall be granted, become exercisable and/or payable and expire, and such other terms and conditions as the Administrator shall determine in its discretion. The Non-Employee Director Equity Compensation Policy may be modified by the Administrator from time to time in its discretion.

4.7 Stand-Alone and Tandem Awards. Awards granted pursuant to the Plan may, in the sole discretion of the Administrator, be granted either alone, in addition to, or in tandem with, any other Award granted pursuant to the Plan. Awards granted in addition to or in tandem with other Awards may be granted either at the same time as or at a different time from the grant of such other Awards.

ARTICLE 5.

PROVISIONS APPLICABLE TO AWARDS INTENDED TO QUALIFY AS PERFORMANCE-BASED COMPENSATION.

5.1 Purpose. The Committee, in its sole discretion, may determine at the time an Award is granted or at any time thereafter whether any Award is intended to qualify as Performance-Based Compensation. If the Committee, in its sole discretion, decides to grant such an Award to an Eligible Individual that is intended to qualify as Performance-Based Compensation, then the provisions of

this Article 5 shall control over any contrary provision contained in the Plan. The Administrator may in its sole discretion grant Awards to other Eligible Individuals that are based on Performance Criteria or Performance Goals but that do not satisfy the requirements of this Article 5 and that are not intended to qualify as Performance-Based Compensation. Unless otherwise specified by the Committee at the time of grant, the Performance Criteria with respect to an Award intended to be Performance-Based Compensation payable to a Covered Employee shall be determined on the basis of Applicable Accounting Standards.

5.2 Applicability. The grant of an Award to an Eligible Individual for a particular Performance Period shall not require the grant of an Award to such Eligible Individual in any subsequent Performance Period and the grant of an Award to any one Eligible Individual shall not require the grant of an Award to any other Eligible Individual in such period or in any other period.

5.3 Types of Awards. Notwithstanding anything in the Plan to the contrary, the Committee may grant any Award to an Eligible Individual intended to qualify as Performance- Based Compensation, including, without limitation, Restricted Stock the restrictions with respect to which lapse upon the attainment of specified Performance Goals, Restricted Stock Units that vest and become payable upon the attainment of specified Performance Goals and any Performance Awards described in Article 10 hereof that vest or become exercisable or payable upon the attainment of one or more specified Performance Goals.

5.4 Procedures with Respect to Performance-Based Awards. To the extent necessary to comply with the requirements of Section 162(m)(4)(C) of the Code, with respect to any Award granted to one or more Eligible Individuals which is intended to qualify as Performance-Based Compensation, no later than ninety (90) days following the commencement of any Performance Period or any designated fiscal period or period of service (or such earlier time as may be required under Section 162(m) of the Code), the Committee shall, in writing, (a) designate one or more Eligible Individuals, (b) select the Performance Criteria applicable to the Performance Period, (c) establish the Performance Goals, and amounts of such Awards, as applicable, which may be earned for such Performance Period based on the Performance Goals, and (d) specify the relationship between the Performance Criteria and the Performance Goals and the amounts of such Awards, as applicable, to be earned by each Covered Employee for such Performance Period. Following the completion of each Performance Period, the Committee shall certify in writing whether and the extent to which the applicable Performance Goals have been achieved for such Performance Period. In determining the amount earned under such Awards, unless otherwise provided in an applicable Program or Award Agreement, the Committee shall have the right to reduce or eliminate (but not to increase) the amount payable at a given level of performance to take into account additional factors that the Committee may deem relevant, including the assessment of individual or corporate performance for the Performance Period.

5.5 Payment of Performance-Based Awards. Unless otherwise provided in the applicable Program or Award Agreement or pursuant to Section 14.2 hereof and only to the extent otherwise permitted by Section 162(m)(4)(C) of the Code, as to an Award that is intended to qualify as Performance-Based Compensation, the Holder must be employed by the Company or an Affiliate throughout the applicable Performance Period. Unless otherwise provided in the applicable Performance Goals, Program or Award Agreement, a Holder shall be eligible to receive payment pursuant to such Awards for a Performance Period only if and to the extent the Performance Goals for such applicable Performance Period are achieved.

5.6 Additional Limitations. Notwithstanding any other provision of the Plan and except as otherwise determined by the Administrator, any Award which is granted to an Eligible Individual and is intended to qualify as Performance-Based Compensation shall be subject to any additional limitations set forth in Section 162(m) of the Code or any regulations or rulings issued thereunder that are requirements for qualification as Performance-Based Compensation, and the Plan, the Program and the Award Agreement shall be deemed amended to the extent necessary to conform to such requirements.

ARTICLE 6.

GRANTING OF OPTIONS

6.1 Granting of Options to Eligible Individuals. The Administrator is authorized to grant Options to Eligible Individuals from time to time, in its sole discretion, on such terms and conditions as it may determine which shall not be inconsistent with the Plan.

6.2 Qualification of Incentive Stock Options. No Incentive Stock Option shall be granted to any person who is not an Employee of the Company or any subsidiary corporation (as defined in Section 424(f) of the Code) of the Company. No person who qualifies as a Greater Than 10% Stockholder may be granted an Incentive Stock Option unless such Incentive Stock Option conforms to the applicable provisions of Section 422 of the Code. Any Incentive Stock Option granted under the Plan may be modified by the Administrator, with the consent of the Holder, to disqualify such Option from treatment as an "incentive stock option" under Section 422 of the Code. To the extent that the aggregate fair market value of stock with respect to which "incentive stock options" (within the meaning of Section 422 of the Code, but without regard to Section 422(d) of the Code) are exercisable for the first time by a Holder during any calendar year under the Plan, and all other plans of the Company and any subsidiary or parent corporation thereof (each as defined in Section 424(f) and (e) of the Code, respectively), exceeds $100,000, the Options shall be treated as Non-Qualified Stock Options to the extent required by Section 422 of the Code. The rule set forth in the preceding sentence shall be applied by taking Options and other "incentive stock options" into account in the order in which they were granted and the Fair Market Value of stock shall be determined as of the time the respective options were granted. In addition, to the extent that any Options otherwise fail to qualify as Incentive Stock Options, such Options shall be treated as Nonqualified Stock Options.

6.3 Option Exercise Price. Except as provided in Article 14 hereof, the exercise price per Share subject to each Option shall be set by the Administrator, but shall not be less than one hundred percent (100%) of the Fair Market Value of a Share on the date the Option is granted (or, as to Incentive Stock Options, on the date the Option is modified, extended or renewed for purposes of Section 424(h) of the Code). In addition, in the case of Incentive Stock Options granted to a Greater Than 10% Stockholder, such price shall not be less than one hundred ten percent (110%) of the Fair Market Value of a Share on the date the Option is granted (or the date the Option is modified, extended or renewed for purposes of Section 424(h) of the Code).

6.4 Option Term. The term of each Option (the "Option Term") shall be set by the Administrator in its sole discretion; provided, however, that the Option Term shall not be more than ten (10) years from the date the Option is granted, or five (5) years from the date an Incentive Stock

Option is granted to a Greater Than 10% Stockholder. The Administrator shall determine the time period, including the time period following a Termination of Service, during which the Holder has the right to exercise the vested Options, which time period may not extend beyond the last day of the Option Term. Except as limited by the requirements of Section 409A or Section 422 of the Code and regulations and rulings thereunder, the Administrator may extend the Option Term of any outstanding Option, may extend the time period during which vested Options may be exercised following any Termination of Service of the Holder, and may amend any other term or condition of such Option relating to such a Termination of Service.

6.5 Option Vesting.

(a) The period during which the right to exercise, in whole or in part, an Option vests in the Holder shall be set by the Administrator and the Administrator may determine that an Option may not be exercised in whole or in part for a specified period after it is granted. Such vesting may be based on service with the Company or any Affiliate, any of the Performance Criteria, or any other criteria selected by the Administrator. At any time after the grant of an Option, the Administrator may, in its sole discretion and subject to whatever terms and conditions it selects, accelerate the vesting of the Option, including following a Termination of Service; provided, that in no event shall an Option become exercisable following its expiration, termination or forfeiture.

(b) No portion of an Option which is unexercisable at a Holder's Termination of Service shall thereafter become exercisable, except as may be otherwise provided by the Administrator either in the Program, the Award Agreement or by action of the Administrator following the grant of the Option.

6.6 Substitute Awards. Notwithstanding the foregoing provisions of this Article 6 to the contrary, in the case of an Option that is a Substitute Award, the price per share of the shares subject to such Option may be less than the Fair Market Value per share on the date of grant; provided that the excess of: (a) the aggregate Fair Market Value (as of the date such Substitute Award is granted) of the shares subject to the Substitute Award, over (b) the aggregate exercise price thereof does not exceed the excess of: (x) the aggregate fair market value (as of the time immediately preceding the transaction giving rise to the Substitute Award, such fair market value to be determined by the Administrator) of the shares of the predecessor entity that were subject to the grant assumed or substituted for by the Company, over (y) the aggregate exercise price of such shares.

6.7 Substitution of Stock Appreciation Rights. The Administrator may provide in the applicable Program or the Award Agreement evidencing the grant of an Option that the Administrator, in its sole discretion, shall have the right to substitute a Stock Appreciation Right for such Option at any time prior to or upon exercise of such Option; provided that such Stock Appreciation Right shall be exercisable with respect to the same number of Shares for which such substituted Option would have been exercisable, and shall also have the same exercise price, vesting schedule and remaining Option Term as the substituted Option.

ARTICLE 7.

EXERCISE OF OPTIONS

7.1 Partial Exercise. An exercisable Option may be exercised in whole or in part. However, an Option shall not be exercisable with respect to fractional Shares and the Administrator may require that, by the terms of the Option, a partial exercise must be with respect to a minimum number of Shares.

7.2 Manner of Exercise. All or a portion of an exercisable Option shall be deemed exercised upon delivery of all of the following to the Secretary of the Company, or such other person or entity designated by the Administrator, or his, her or its office, as applicable:

(a) A written or electronic notice complying with the applicable rules established by the Administrator stating that the Option, or a portion thereof, is exercised. The notice shall be signed by the Holder or other person then entitled to exercise the Option or such portion of the Option;

(b) Such representations and documents as the Administrator, in its sole discretion, deems necessary or advisable to effect compliance with all Applicable Law. The Administrator may, in its sole discretion, also take whatever additional actions it deems appropriate to effect such compliance including, without limitation, placing legends on share certificates and issuing stop-transfer notices to agents and registrars;

(c) In the event that the Option shall be exercised pursuant to Section 12.3 hereof by any person or persons other than the Holder, appropriate proof of the right of such person or persons to exercise the Option, as determined in the sole discretion of the Administrator; and

(d) Full payment of the exercise price and applicable withholding taxes to the stock administrator of the Company for the shares with respect to which the Option, or portion thereof, is exercised, in a manner permitted by Section 12.1 and 12.2 hereof.

7.3 Notification Regarding Disposition. The Holder shall give the Company prompt written or electronic notice of any disposition of Shares acquired by exercise of an Incentive Stock Option which occurs within (a) two (2) years from the date of granting (including the date the Option is modified, extended or renewed for purposes of Section 424(h) of the Code) of such Option to such Holder, or (b) one (1) year after the transfer of such shares to such Holder.

ARTICLE 8.

AWARD OF RESTRICTED STOCK

8.1 Award of Restricted Stock.

(a) The Administrator is authorized to grant Restricted Stock to Eligible Individuals, and shall determine the terms and conditions, including the restrictions applicable to each award of Restricted Stock, which terms and conditions shall not be inconsistent with the Plan, and may impose such conditions on the issuance of such Restricted Stock as it deems appropriate.

(b) The Administrator shall establish the purchase price, if any, and form of payment for Restricted Stock; provided, however, that if a purchase price is charged, such purchase price shall be no less than the par value, if any, of the Shares to be purchased, unless otherwise permitted by Applicable Law. In all cases, legal consideration shall be required for each issuance of Restricted Stock to the extent required by Applicable Law.

8.2 Rights as Stockholders. Subject to Section 8.4 hereof, upon issuance of Restricted Stock, the Holder shall have, unless otherwise provided by the Administrator, all the rights of a stockholder with respect to said Shares, subject to the restrictions in the applicable Program or in each individual Award Agreement, including the right to receive all dividends and other distributions paid or made with respect to the Shares; provided, however, that, in the sole discretion of the Administrator, any extraordinary distributions with respect to the Shares shall be subject to the restrictions set forth in Section 8.3 hereof. In addition, with respect to a share of Restricted Stock with performance-based vesting, dividends which are paid prior to vesting shall only be paid out to the Holder to the extent that performance-based vesting conditions are subsequently satisfied and the share of Restricted Stock vests.

8.3 Restrictions. All shares of Restricted Stock (including any shares received by Holders thereof with respect to shares of Restricted Stock as a result of stock dividends, stock splits or any other form of recapitalization) shall, in the terms of the applicable Program or in each individual Award Agreement, be subject to such restrictions and vesting requirements as the Administrator shall provide. Such restrictions may include, without limitation, restrictions concerning voting rights and transferability and such restrictions may lapse separately or in combination at such times and pursuant to such circumstances or based on such criteria as selected by the Administrator, including, without limitation, criteria based on the Holder's duration of employment, directorship or consultancy with the Company, the Performance Criteria, Company or Affiliate performance, individual performance or other criteria selected by the Administrator. By action taken after the Restricted Stock is issued, the Administrator may, on such terms and conditions as it may determine to be appropriate, accelerate the vesting of such Restricted Stock by removing any or all of the restrictions imposed by the terms of the Program and/or the Award Agreement. Restricted Stock may not be sold or encumbered until all restrictions are terminated or expire.

8.4 Repurchase or Forfeiture of Restricted Stock. Except as otherwise determined by the Administrator at the time of the grant of the Award or thereafter, if no price was paid by the Holder for the Restricted Stock, upon a Termination of Service during the applicable restriction period, the Holder's rights in unvested Restricted Stock then subject to restrictions shall lapse, and such

Restricted Stock shall be surrendered to the Company and cancelled without consideration. If a price was paid by the Holder for the Restricted Stock, upon a Termination of Service during the applicable restriction period, the Company shall have the right to repurchase from the Holder the unvested Restricted Stock then subject to restrictions at a cash price per share equal to the price paid by the Holder for such Restricted Stock or such other amount as may be specified in the Program or the Award Agreement. Notwithstanding the foregoing, the Administrator in its sole discretion may provide that in the event of certain events, including a Change in Control, the Holder's death, retirement or disability or any other specified Termination of Service or any other event, the Holder's rights in unvested Restricted Stock shall not lapse, such Restricted Stock shall vest and, if applicable, the Company shall not have a right of repurchase.

8.5 Certificates for Restricted Stock. Restricted Stock granted pursuant to the Plan may be evidenced in such manner as the Administrator shall determine. Certificates or book entries evidencing shares of Restricted Stock must include an appropriate legend referring to the terms, conditions, and restrictions applicable to such Restricted Stock. The Company may, in it sole discretion, (a) retain physical possession of any stock certificate evidencing shares of Restricted Stock until the restrictions thereon shall have lapsed and/or (b) require that the stock certificates evidencing shares of Restricted Stock be held in custody by a designated escrow agent (which may but need not be the Company) until the restrictions thereon shall have lapsed, and that the Holder deliver a stock power, endorsed in blank, relating to such Restricted Stock.

8.6 Section 83(b) Election. If a Holder makes an election under Section 83(b) of the Code to be taxed with respect to the Restricted Stock as of the date of transfer of the Restricted Stock rather than as of the date or dates upon which the Holder would otherwise be taxable under Section 83(a) of the Code, the Holder shall be required to deliver a copy of such election to the Company promptly after filing such election with the Internal Revenue Service.

ARTICLE 9.

AWARD OF RESTRICTED STOCK UNITS

9.1 Grant of Restricted Stock Units. The Administrator is authorized to grant Awards of Restricted Stock Units to any Eligible Individual selected by the Administrator in such amounts and subject to such terms and conditions as determined by the Administrator.

9.2 Term. Except as otherwise provided herein, the term of a Restricted Stock Unit award shall be set by the Administrator in its sole discretion.

9.3 Purchase Price. The Administrator shall specify the purchase price, if any, to be paid by the Holder to the Company with respect to any Restricted Stock Unit award; provided, however, that value of the consideration shall not be less than the par value of a Share, unless otherwise permitted by Applicable Law.

9.4 Vesting of Restricted Stock Units. At the time of grant, the Administrator shall specify the date or dates on which the Restricted Stock Units shall become fully vested and nonforfeitable, and may specify such conditions to vesting as it deems appropriate, including, without limitation, vesting based upon the Holder's duration of service to the Company or any

Affiliate, one or more Performance Criteria, Company performance, individual performance or other specific criteria, in each case on a specified date or dates or over any period or periods, as determined by the Administrator.

9.5 Maturity and Payment. At the time of grant, the Administrator shall specify the maturity date applicable to each grant of Restricted Stock Units which shall be no earlier than the vesting date or dates of the Award and may be determined at the election of the Holder (if permitted by the applicable Award Agreement); provided that, except as otherwise determined by the Administrator, set forth in any applicable Award Agreement, and subject to compliance with Section 409A of the Code, in no event shall the maturity date relating to each Restricted Stock Unit occur following the later of (a) the fifteenth (15th) day of the third (3rd) month following the end of calendar year in which the Restricted Stock Unit vests; or (b) the fifteenth (15th) day of the third (3rd) month following the end of the Company's fiscal year in which the Restricted Stock Unit vests. On the maturity date, the Company shall, subject to Section 12.4(e) hereof, transfer to the Holder one unrestricted, fully transferable Share for each Restricted Stock Unit scheduled to be paid out on such date and not previously forfeited, or, in the sole discretion of the Administrator, an amount in cash equal to the Fair Market Value of such shares on the maturity date or a combination of cash and Common Stock as determined by the Administrator.

9.6 Payment upon Termination of Service. An Award of Restricted Stock Units shall only be payable while the Holder is an Employee, a Consultant or a member of the Board, as applicable; provided, however, that the Administrator, in its sole and absolute discretion may provide (in an Award Agreement or otherwise) that a Restricted Stock Unit award may be paid subsequent to a Termination of Service in certain events, including a Change in Control, the Holder's death, retirement or disability or any other specified Termination of Service.

9.7 No Rights as a Stockholder. Unless otherwise determined by the Administrator, a Holder who is awarded Restricted Stock Units shall possess no incidents of ownership with respect to the Shares represented by such Restricted Stock Units, unless and until the same are transferred to the Holder pursuant to the terms of this Plan and the Award Agreement.

9.8 Dividend Equivalents. Subject to Section 10.2 hereof, the Administrator may, in its sole discretion, provide that Dividend Equivalents shall be earned by a Holder of Restricted Stock Units based on dividends declared on the Common Stock, to be credited as of dividend payment dates during the period between the date an Award of Restricted Stock Units is granted to a Holder and the maturity date of such Award.

ARTICLE 10.

AWARD OF PERFORMANCE AWARDS, DIVIDEND EQUIVALENTS, STOCK PAYMENTS, DEFERRED STOCK, DEFERRED STOCK UNITS

10.1 Performance Awards.

(a) The Administrator is authorized to grant Performance Awards, including Awards of Performance Stock Units, to any Eligible Individual and to determine

whether such Performance Awards shall be Performance-Based Compensation. The value of Performance Awards, including Performance Stock Units, may be linked to any one or more of the Performance Criteria or other specific criteria determined by the Administrator, in each case on a specified date or dates or over any period or periods determined by the Administrator. Performance Awards, including Performance Stock Unit awards may be paid in cash, Shares, or a combination of cash and Shares, as determined by the Administrator.

(b) Without limiting Section 10.1(a) hereof, the Administrator may grant Performance Awards to any Eligible Individual in the form of a cash bonus payable upon the attainment of objective Performance Goals, or such other criteria, whether or not objective, which are established by the Administrator, in each case on a specified date or dates or over any period or periods determined by the Administrator. Any such bonuses paid to a Holder which are intended to be Performance-Based Compensation shall be based upon objectively determinable bonus formulas established in accordance with the provisions of Article 5 hereof.

10.2 Dividend Equivalents.

(a) Dividend Equivalents may be granted by the Administrator based on dividends declared on the Common Stock, to be credited as of dividend payment dates during the period between the date an Award is granted to a Holder and the date such Award vests, is exercised, is distributed or expires, as determined by the Administrator. Such Dividend Equivalents shall be converted to cash or additional shares of Common Stock by such formula and at such time and subject to such limitations as may be determined by the Administrator. In addition, Dividend Equivalents with respect to an Award with performance-based vesting that are based on dividends paid prior to the vesting of such Award shall only be paid out to Holder to the extent that the performance-based vesting conditions are subsequently satisfied and the Award vests.

(b) Notwithstanding the foregoing, no Dividend Equivalents shall be payable with respect to Options or Stock Appreciation Rights.

10.3 Stock Payments. The Administrator is authorized to make Stock Payments to any Eligible Individual. The number or value of Shares of any Stock Payment shall be determined by the Administrator and may be based upon one or more Performance Criteria or any other specific criteria, including service to the Company or any Affiliate, determined by the Administrator. Shares underlying a Stock Payment which is subject to a vesting schedule or other conditions or criteria set by the Administrator will not be issued until those conditions have been satisfied. Unless otherwise provided by the Administrator, a Holder of a Stock Payment shall have no rights as a Company stockholder with respect to such Stock Payment until such time as the Stock Payment has vested and the Shares underlying the Award have been issued to the Holder. Stock Payments may, but are not required to, be made in lieu of base salary, bonus, fees or other cash compensation otherwise payable to such Eligible Individual.

10.4 Deferred Stock. The Administrator is authorized to grant Deferred Stock to any Eligible Individual. The number of shares of Deferred Stock shall be determined by the

Administrator and may (but is not required to) be based on one or more Performance Criteria or other specific criteria, including service to the Company or any Affiliate, as the Administrator determines, in each case on a specified date or dates or over any period or periods determined by the Administrator. Shares underlying a Deferred Stock award which is subject to a vesting schedule or other conditions or criteria set by the Administrator will be issued on the vesting date(s) or date(s) that those conditions and criteria have been satisfied, as applicable. Unless otherwise provided by the Administrator, a Holder of Deferred Stock shall have no rights as a Company stockholder with respect to such Deferred Stock until such time as the Award has vested and any other applicable conditions and/or criteria have been satisfied and the Shares underlying the Award have been issued to the Holder.

10.5 Deferred Stock Units. The Administrator is authorized to grant Deferred Stock Units to any Eligible Individual. The number of Deferred Stock Units shall be determined by the Administrator and may (but is not required to) be based on one or more Performance Criteria or other specific criteria, including service to the Company or any Affiliate, as the Administrator determines, in each case on a specified date or dates or over any period or periods determined by the Administrator. Each Deferred Stock Unit shall entitle the Holder thereof to receive one share of Common Stock on the date the Deferred Stock Unit becomes vested or upon a specified settlement date thereafter (which settlement date may (but is not required to) be the date of the Holder's Termination of Service). Shares underlying a Deferred Stock Unit award which is subject to a vesting schedule or other conditions or criteria set by the Administrator will not be issued until on or following the date that those conditions and criteria have been satisfied. Unless otherwise provided by the Administrator, a Holder of Deferred Stock Units shall have no rights as a Company stockholder with respect to such Deferred Stock Units until such time as the Award has vested and any other applicable conditions and/or criteria have been satisfied and the Shares underlying the Award have been issued to the Holder.

10.6 Term. The term of a Performance Award, Dividend Equivalent award, Stock Payment award, Deferred Stock award and/or Deferred Stock Unit award shall be set by the Administrator in its sole discretion.

10.7 Purchase Price. The Administrator may establish the purchase price of a Performance Award, Shares distributed as a Stock Payment award, shares of Deferred Stock or Shares distributed pursuant to a Deferred Stock Unit award; provided, however, that value of the consideration shall not be less than the par value of a Share, unless otherwise permitted by Applicable Law.

10.8 Termination of Service. A Performance Award, Stock Payment award, Dividend Equivalent award, Deferred Stock award and/or Deferred Stock Unit award is distributable only while the Holder is an Employee, Director or Consultant, as applicable. The Administrator, however, in its sole discretion may provide that the Performance Award, Dividend Equivalent award, Stock Payment award, Deferred Stock award and/or Deferred Stock Unit award may be distributed subsequent to a Termination of Service in certain events, including a Change in Control, the Holder's death, retirement or disability or any other specified Termination of Service.

ARTICLE 11.

AWARD OF STOCK APPRECIATION RIGHTS

11.1 Grant of Stock Appreciation Rights.

(a) The Administrator is authorized to grant Stock Appreciation Rights to Eligible Individuals from time to time, in its sole discretion, on such terms and conditions as it may determine consistent with the Plan.

(b) A Stock Appreciation Right shall entitle the Holder (or other person entitled to exercise the Stock Appreciation Right pursuant to the Plan) to exercise all or a specified portion of the Stock Appreciation Right (to the extent then exercisable pursuant to its terms) and to receive from the Company an amount determined by multiplying the difference obtained by subtracting the exercise price per Share of the Stock Appreciation Right from the Fair Market Value on the date of exercise of the Stock Appreciation Right by the number of Shares with respect to which the Stock Appreciation Right shall have been exercised, subject to any limitations the Administrator may impose. Except as described in (c) below or in Section 14.2 hereof, the exercise price per Share subject to each Stock Appreciation Right shall be set by the Administrator, but shall not be less than one hundred percent (100%) of the Fair Market Value on the date the Stock Appreciation Right is granted.

(c) Notwithstanding the foregoing provisions of Section 11.1(b) hereof to the contrary, in the case of a Stock Appreciation Right that is a Substitute Award, the price per Share of the Shares subject to such Stock Appreciation Right may be less than one hundred percent (100%) of the Fair Market Value per share on the date of grant; provided that the excess of: (i) the aggregate Fair Market Value (as of the date such Substitute Award is granted) of the shares subject to the Substitute Award, over (ii) the aggregate exercise price thereof does not exceed the excess of: (x) the aggregate fair market value (as of the time immediately preceding the transaction giving rise to the Substitute Award, such fair market value to be determined by the Administrator) of the shares of the predecessor entity that were subject to the grant assumed or substituted for by the Company, over (y) the aggregate exercise price of such shares.

11.2 Stock Appreciation Right Vesting.

(a) The period during which the right to exercise, in whole or in part, a Stock Appreciation Right vests in the Holder shall be set by the Administrator and the Administrator may determine that a Stock Appreciation Right may not be exercised in whole or in part for a specified period after it is granted. Such vesting may be based on service with the Company or any Affiliate, any of the Performance Criteria or any other criteria selected by the Administrator. At any time after grant of a Stock Appreciation Right, the Administrator may, in its sole discretion and subject to whatever terms and conditions it selects, accelerate the period during which a Stock Appreciation Right vests.

(b) No portion of a Stock Appreciation Right which is unexercisable at Termination of Service shall thereafter become exercisable, except as may be otherwise

provided by the Administrator either in the applicable Program or Award Agreement or by action of the Administrator following the grant of the Stock Appreciation Right, including following a Termination of Service; provided, that in no event shall a Stock Appreciation Right become exercisable following its expiration, termination or forfeiture.

11.3 Manner of Exercise. All or a portion of an exercisable Stock Appreciation Right shall be deemed exercised upon delivery of all of the following to the stock administrator of the Company, or such other person or entity designated by the Administrator, or his, her or its office, as applicable:

(a) A written or electronic notice complying with the applicable rules established by the Administrator stating that the Stock Appreciation Right, or a portion thereof, is exercised. The notice shall be signed by the Holder or other person then entitled to exercise the Stock Appreciation Right or such portion of the Stock Appreciation Right;

(b) Such representations and documents as the Administrator, in its sole discretion, deems necessary or advisable to effect compliance with all applicable provisions of the Securities Act and any other federal, state or foreign securities laws or regulations. The Administrator may, in its sole discretion, also take whatever additional actions it deems appropriate to effect such compliance; and

(c) In the event that the Stock Appreciation Right shall be exercised pursuant to this Section 11.3 hereof by any person or persons other than the Holder, appropriate proof of the right of such person or persons to exercise the Stock Appreciation Right.

11.4 Stock Appreciation Right Term. The term of each Stock Appreciation Right (the "Stock Appreciation Right Term") shall be set by the Administrator in its sole discretion; provided, however, that the term shall not be more than ten (10) years from the date the Stock Appreciation Right is granted. The Administrator shall determine the time period, including the time period following a Termination of Service, during which the Holder has the right to exercise the vested Stock Appreciation Rights, which time period may not extend beyond the expiration date of the Stock Appreciation Right Term. Except as limited by the requirements of Section 409A of the Code and regulations and rulings thereunder or the first sentence of this Section 11.4, the Administrator may extend the Stock Appreciation Right Term of any outstanding Stock Appreciation Right, may extend the time period during which vested Stock Appreciation Rights may be exercised following any Termination of Service of the Holder, and may amend any other term or condition of such Stock Appreciation Right relating to such a Termination of Service.

11.5 Payment. Payment of the amounts payable with respect to Stock Appreciation Rights pursuant to this Article 11 shall be in cash, Shares (based on its Fair Market Value as of the date the Stock Appreciation Right is exercised), or a combination of both, as determined by the Administrator.

ARTICLE 12.

ADDITIONAL TERMS OF AWARDS

12.1 Payment. The Administrator shall determine the methods by which payments by any Holder with respect to any Awards granted under the Plan shall be made, including, without limitation: (a) cash or check, (b) Shares (including, in the case of payment of the exercise price of an Award, Shares issuable pursuant to the exercise of the Award) or Shares held for such period of time as may be required by the Administrator in order to avoid adverse accounting consequences, in each case, having a Fair Market Value on the date of delivery equal to the aggregate payments required, (c) delivery of a written or electronic notice that the Holder has placed a market sell order with a broker with respect to Shares then issuable upon exercise or vesting of an Award, and that the broker has been directed to pay a sufficient portion of the net proceeds of the sale to the Company in satisfaction of the aggregate payments required; provided that payment of such proceeds is then made to the Company upon settlement of such sale, or (d) other form of legal consideration acceptable to the Administrator. The Administrator shall also determine the methods by which Shares shall be delivered or deemed to be delivered to Holders. Notwithstanding any other provision of the Plan to the contrary, no Holder who is a Director or an "executive officer" of the Company within the meaning of Section 13(k) of the Exchange Act shall be permitted to make payment with respect to any Awards granted under the Plan, or continue any extension of credit with respect to such payment, with a loan from the Company or a loan arranged by the Company in violation of Section 13(k) of the Exchange Act.

12.2 Tax Withholding. The Company or any Affiliate shall have the authority and the right to deduct or withhold, or require a Holder to remit to the Company, an amount sufficient to satisfy federal, state, local and foreign taxes (including the Holder's FICA or employment tax obligation) required by law to be withheld with respect to any taxable event concerning a Holder arising as a result of the Plan. The Administrator may in its sole discretion and in satisfaction of the foregoing requirement allow a Holder to satisfy such obligations by any payment means described in Section 12.1 hereof, including without limitation, by allowing such Holder to elect to have the Company withhold Shares otherwise issuable under an Award (or allow the surrender of Shares). The number of Shares which may be so withheld or surrendered shall be limited to the number of Shares which have a Fair Market Value on the date of withholding or repurchase equal to the aggregate amount of such liabilities based on the minimum statutory withholding rates for federal, state, local and foreign income tax and payroll tax purposes that are applicable to such supplemental taxable income. The Administrator shall determine the fair market value of the Shares, consistent with applicable provisions of the Code, for tax withholding obligations due in connection with a broker-assisted cashless Option or Stock Appreciation Right exercise involving the sale of Shares to pay the Option or Stock Appreciation Right exercise price or any tax withholding obligation.

12.3 Transferability of Awards.

(a) Except as otherwise provided in Sections 12.3(b) and 12.3(c) hereof:

(i) No Award under the Plan may be sold, pledged, assigned or transferred in any manner other than by will or the laws of descent and distribution or, subject to the consent of the Administrator, pursuant to a DRO, unless and until such Award has been exercised, or the Shares underlying such Award have been issued, and all restrictions applicable to such Shares have lapsed;

(ii) No Award or interest or right therein shall be liable for the debts, contracts or engagements of the Holder or the Holder's successors in interest or shall be subject to disposition by transfer, alienation, anticipation, pledge, hypothecation, encumbrance, assignment or any other means whether such disposition be voluntary or involuntary or by operation of law by judgment, levy, attachment, garnishment or any other legal or equitable proceedings (including bankruptcy) unless and until such Award has been exercised, or the Shares underlying such Award have been issued, and all restrictions applicable to such Shares have lapsed, and any attempted disposition of an Award prior to the satisfaction of these conditions shall be null and void and of no effect, except to the extent that such disposition is permitted by clause (i) of this provision; and

(iii) During the lifetime of the Holder, only the Holder may exercise an Award (or any portion thereof) granted to such Holder under the Plan, unless it has been disposed of pursuant to a DRO; after the death of the Holder, any exercisable portion of an Award may, prior to the time when such portion becomes unexercisable under the Plan or the applicable Program or Award Agreement, be exercised by the Holder's personal representative or by any person empowered to do so under the deceased Holder's will or under the then applicable laws of descent and distribution.

(b) Notwithstanding Section 12.3(a) hereof, the Administrator, in its sole discretion, may determine to permit a Holder or a Permitted Transferee of such Holder to transfer an Award other than an Incentive Stock Option (unless such Incentive Stock Option is to become a Non-Qualified Stock Option) to any one or more Permitted Transferees, subject to the following terms and conditions: (i) an Award transferred to a Permitted Transferee shall not be assignable or transferable by the Permitted Transferee (other than to another Permitted Transferee of the applicable Holder) other than by will or the laws of descent and distribution; (ii) an Award transferred to a Permitted Transferee shall continue to be subject to all the terms and conditions of the Award as applicable to the original Holder (other than the ability to further transfer the Award); and (iii) the Holder (or transferring Permitted Transferee) and the Permitted Transferee shall execute any and all documents requested by the Administrator, including, without limitation documents to (A) confirm the status of the transferee as a Permitted Transferee, (B) satisfy any requirements for an exemption for the transfer under applicable federal, state and foreign securities laws and (C) evidence the transfer.

(c) Notwithstanding Section 12.3(a) hereof, a Holder may, in the manner determined by the Administrator, designate a beneficiary to exercise the rights of the Holder and to receive any distribution with respect to any Award upon the Holder's death. A beneficiary, legal guardian, legal representative, or other person claiming any rights pursuant to the Plan is subject to all terms and conditions of the Plan and any Program or Award Agreement applicable to the Holder, except to the extent the Plan, the Program and the Award Agreement otherwise provide, and to any additional restrictions deemed necessary or

appropriate by the Administrator. If the Holder is married or a domestic partner in a domestic partnership qualified under Applicable Law and resides in a community property state, a designation of a person other than the Holder's spouse or domestic partner, as applicable, as his or her beneficiary with respect to more than fifty percent (50%) of the Holder's interest in the Award shall not be effective without the prior written or electronic consent of the Holder's spouse or domestic partner, as applicable. If no beneficiary has been designated or survives the Holder, payment shall be made to the person entitled thereto pursuant to the Holder's will or the laws of descent and distribution. Subject to the foregoing, a beneficiary designation may be changed or revoked by a Holder at any time; provided that the change or revocation is filed with the Administrator prior to the Holder's death.

12.4 Conditions to Issuance of Shares.

(a) Notwithstanding anything herein to the contrary, the Company shall not be required to issue or deliver any certificates or make any book entries evidencing Shares pursuant to the exercise of any Award, unless and until the Board or the Committee has determined, with advice of counsel, that the issuance of such shares is in compliance with all Applicable Law, and the Shares are covered by an effective registration statement or applicable exemption from registration. In addition to the terms and conditions provided herein, the Board or the Committee may require that a Holder make such reasonable covenants, agreements, and representations as the Board or the Committee, in its discretion, deems advisable in order to comply with Applicable Law.

(b) All Share certificates delivered pursuant to the Plan and all Shares issued pursuant to book entry procedures are subject to any stop-transfer orders and other restrictions as the Administrator deems necessary or advisable to comply with Applicable Law. The Administrator may place legends on any Share certificate or book entry to reference restrictions applicable to the Shares.

(c) The Administrator shall have the right to require any Holder to comply with any timing or other restrictions with respect to the settlement, distribution or exercise of any Award, including a window-period limitation, as may be imposed in the sole discretion of the Administrator.

(d) No fractional Shares shall be issued and the Administrator shall determine, in its sole discretion, whether cash shall be given in lieu of fractional Shares or whether such fractional Shares shall be eliminated by rounding down.

(e) Notwithstanding any other provision of the Plan, unless otherwise determined by the Administrator or required by any Applicable Law, the Company shall not deliver to any Holder certificates evidencing Shares issued in connection with any Award and instead such Shares shall be recorded in the books of the Company (or, as applicable, its transfer agent or stock plan administrator).

12.5 Forfeiture and Claw-Back Provisions. Pursuant to its general authority to determine the terms and conditions applicable to Awards under the Plan, the Administrator shall have the right

to provide, in an Award Agreement or otherwise, or to require a Holder to agree by separate written or electronic instrument, that:

(a) (i) Any proceeds, gains or other economic benefit actually or constructively received by the Holder upon any receipt or exercise of the Award, or upon the receipt or resale of any Shares underlying the Award, must be paid to the Company, and (ii) the Award shall terminate and any unexercised portion of the Award (whether or not vested) shall be forfeited, if (x) a Termination of Service occurs prior to a specified date, or within a specified time period following receipt or exercise of the Award, or (y) the Holder at any time, or during a specified time period, engages in any activity in competition with the Company, or which is inimical, contrary or harmful to the interests of the Company, as further defined by the Administrator or (z) the Holder incurs a Termination of Service for "cause" (as such term is defined in the sole discretion of the Administrator, or as set forth in a written agreement relating to such Award between the Company and the Holder); and

(b) All Awards (including any proceeds, gains or other economic benefit actually or constructively received by the Holder upon any receipt or exercise of any Award or upon the receipt or resale of any Shares underlying the Award) shall be subject to the provisions of any claw-back policy implemented by the Company, including, without limitation, any claw- back policy adopted to comply with the requirements of Applicable Law, including, without limitation, the Dodd-Frank Wall Street Reform and Consumer Protection Act and any rules or regulations promulgated thereunder, to the extent set forth in such claw-back policy and/or in the applicable Award Agreement.

12.6 Prohibition on Repricing. Subject to Section 14.2 hereof, the Administrator shall not, without the approval of the stockholders of the Company, (i) authorize the amendment of any outstanding Option or Stock Appreciation Right to reduce its price per Share, or (ii) cancel any Option or Stock Appreciation Right in exchange for cash or another Award when the Option or Stock Appreciation Right price per Share exceeds the Fair Market Value of the underlying Shares.

12.7 Leave of Absence. Unless the Administrator provides otherwise, vesting of Awards granted hereunder shall be suspended during any unpaid leave of absence. A Holder shall not cease to be considered an Employee, Non-Employee Director or Consultant, as applicable, in the case of any (a) leave of absence approved by the Company, (b) transfer between locations of the Company or between the Company and any of its Affiliates or any successor thereof, or (c) change in status (Employee to Director, Employee to Consultant, etc.), provided that such change does not affect the specific terms applying to the Holder's Award.

ARTICLE 13.

ADMINISTRATION

13.1 Administrator. The Committee (or another committee or a subcommittee of the Board or the Compensation Committee of the Board assuming the functions of the Committee under the Plan) shall administer the Plan (except as otherwise permitted herein) and, unless otherwise determined by the Board, shall consist solely of two or more Non-Employee Directors appointed by

and holding office at the pleasure of the Board, each of whom is intended to qualify as both a "non-employee director" as defined by Rule 16b-3 of the Exchange Act or any successor rule, an "outside director" for purposes of Section 162(m) of the Code and an "independent director" under the rules of any securities exchange or automated quotation system on which the Shares are listed, quoted or traded; provided that any action taken by the Committee shall be valid and effective, whether or not members of the Committee at the time of such action are later determined not to have satisfied the requirements for membership set forth in this Section 13.1 or otherwise provided in any charter of the Committee. Except as may otherwise be provided in any charter of the Committee, appointment of Committee members shall be effective upon acceptance of appointment. Committee members may resign at any time by delivering written or electronic notice to the Board. Vacancies in the Committee may only be filled by the Board. Notwithstanding the foregoing, (a) the full Board, acting by a majority of its members in office, shall conduct the general administration of the Plan with respect to Awards granted to Non-Employee Directors and, with respect to such Awards, the terms "Administrator" and "Committee" as used in the Plan shall be deemed to refer to the Board and (b) the Board or Committee may delegate its authority hereunder to the extent permitted by Section 13.6 hereof.

13.2 Duties and Powers of Administrator. It shall be the duty of the Administrator to conduct the general administration of the Plan in accordance with its provisions. The Administrator shall have the power to interpret the Plan, the Program and the Award Agreement, and to adopt such rules for the administration, interpretation and application of the Plan as are not inconsistent therewith, to interpret, amend or revoke any such rules and to amend any Program or Award Agreement; provided that the rights or obligations of the Holder of the Award that is the subject of any such Program or Award Agreement are not affected materially and adversely by such amendment, unless the consent of the Holder is obtained or such amendment is otherwise permitted under Section 14.10 hereof. Any such grant or award under the Plan need not be the same with respect to each Holder. Any such interpretations and rules with respect to Incentive Stock Options shall be consistent with the provisions of Section 422 of the Code. In its sole discretion, the Board may at any time and from time to time exercise any and all rights and duties of the Committee under the Plan except with respect to matters which under Rule 16b-3 under the Exchange Act or any successor rule, or Section 162(m) of the Code, or any regulations or rules issued thereunder, or the rules of any securities exchange or automated quotation system on which the Shares are listed, quoted or traded are required to be determined in the sole discretion of the Committee.

13.3 Action by the Committee. Unless otherwise established by the Board or in any charter of the Committee, a majority of the Committee shall constitute a quorum and the acts of a majority of the members present at any meeting at which a quorum is present, and acts approved in writing by all members of the Committee in lieu of a meeting, shall be deemed the acts of the Committee. Each member of the Committee is entitled to, in good faith, rely or act upon any report or other information furnished to that member by any officer or other employee of the Company or any Affiliate, the Company's independent certified public accountants, or any executive compensation consultant or other professional retained by the Company to assist in the administration of the Plan.

13.4 Authority of Administrator. Subject to the Company's Bylaws, the Committee's Charter and any specific designation in the Plan, the Administrator has the exclusive power, authority and sole discretion to:

(a) Designate Eligible Individuals to receive Awards;

(b) Determine the type or types of Awards to be granted to each Eligible Individual;

(c) Determine the number of Awards to be granted and the number of Shares to which an Award will relate;

(d) Determine the terms and conditions of any Award granted pursuant to the Plan, including, but not limited to, the exercise price, grant price, or purchase price, any performance criteria, any restrictions or limitations on the Award, any schedule for vesting, lapse of forfeiture restrictions or restrictions on the exercisability of an Award, and accelerations or waivers thereof, and any provisions related to non-competition and recapture of gain on an Award, based in each case on such considerations as the Administrator in its sole discretion determines;

(e) Determine whether, to what extent, and pursuant to what circumstances an Award may be settled in, or the exercise price of an Award may be paid in cash, Shares, other Awards, or other property, or an Award may be canceled, forfeited, or surrendered;

(f) Prescribe the form of each Award Agreement, which need not be identical for each Holder;

(g) Decide all other matters that must be determined in connection with an Award;

(h) Establish, adopt, or revise any rules and regulations as it may deem necessary or advisable to administer the Plan;

(i) Interpret the terms of, and any matter arising pursuant to, the Plan, any Program or any Award Agreement;

(j) Make all other decisions and determinations that may be required pursuant to the Plan or as the Administrator deems necessary or advisable to administer the Plan; and

(k) Accelerate wholly or partially the vesting or lapse of restrictions of any Award or portion thereof at any time after the grant of an Award, subject to whatever terms and conditions it selects and Sections 3.4 and 14.2(d) hereof.

13.5 Decisions Binding. The Administrator's interpretation of the Plan, any Awards granted pursuant to the Plan, any Program, any Award Agreement and all decisions and determinations by the Administrator with respect to the Plan are final, binding, and conclusive on all parties.

13.6 Delegation of Authority. To the extent permitted by Applicable Law, the Board or Committee may from time to time delegate to a committee of one or more members of the Board or one or more officers of the Company the authority to grant or amend Awards or to take other administrative actions pursuant to Article 13; provided, however, that in no event shall an officer of the Company be delegated the authority to grant awards to, or amend awards held by, the following individuals: (a) individuals who are subject to Section 16 of the Exchange Act, (b) Covered Employees, or (c) officers of the Company (or Directors) to whom authority to grant or amend Awards has been delegated hereunder; provided, further, that any delegation of administrative authority shall only be permitted to the extent it is permissible under Section 162(m) of the Code

and Applicable Law. Any delegation hereunder shall be subject to the restrictions and limits that the Board or Committee specifies at the time of such delegation, and the Board may at any time rescind the authority so delegated or appoint a new delegatee. At all times, the delegatee appointed under this Section 13.6 hereof shall serve in such capacity at the pleasure of the Board and the Committee.

ARTICLE 14.

MISCELLANEOUS PROVISIONS

14.1 Amendment, Suspension or Termination of the Plan. Except as otherwise provided in this Section 14.1, the Plan may be wholly or partially amended or otherwise modified, suspended or terminated at any time or from time to time by the Board or the Committee. However, without approval of the Company's stockholders given within twelve (12) months before or after the action by the Administrator, no action of the Administrator may, except as provided in Section 14.2 hereof, (a) increase the limits imposed in Section 3.1 hereof on the maximum number of shares which may be issued under the Plan, or (b) reduce the price per share of any outstanding Option or Stock Appreciation Right granted under the Plan, or (c) cancel any Option or Stock Appreciation Right in exchange for cash or another Award when the Option or Stock Appreciation Right price per share exceeds the Fair Market Value of the underlying Shares. Except as provided in Section 14.10 hereof, no amendment, suspension or termination of the Plan shall, without the consent of the Holder, materially and adversely affect any rights or obligations under any Award theretofore granted or awarded, unless the Award itself otherwise expressly so provides. No Awards may be granted or awarded during any period of suspension or after termination of the Plan, and in no event may any Award be granted under the Plan after the tenth (10th) anniversary of the Effective Date.

14.2 Changes in Common Stock or Assets of the Company, Acquisition or Liquidation of the Company and Other Corporate Events.

(a) In the event of any stock dividend, stock split, combination or exchange of shares, merger, consolidation or other distribution (other than normal cash dividends) of Company assets to stockholders, or any other change affecting the shares of the Company's stock or the share price of the Company's stock other than an Equity Restructuring, the Administrator may make equitable adjustments, if any, to reflect such change with respect to (i) the aggregate number and kind of shares that may be issued under the Plan (including, but not limited to, adjustments of the limitations in Section 3.1 hereof on the maximum number and kind of shares which may be issued under the Plan); (ii) the number and kind of shares of Common Stock (or other securities or property) subject to outstanding Awards; (iii) the number and kind of shares of Common Stock (or other securities or property) for which grants are subsequently to be made to new and continuing Non-Employee Directors pursuant to Section 4.6 hereof; (iv) the terms and conditions of any outstanding Awards (including, without limitation, any applicable performance targets or criteria with respect thereto); and (v) the grant or exercise price per share for any outstanding Awards under the Plan. Any adjustment affecting an Award intended as Performance-Based Compensation shall be made consistent with the requirements of Section 162(m) of the Code.

(b) In the event of any transaction or event described in Section 14.2(a) hereof or any unusual or nonrecurring transactions or events affecting the Company, any Affiliate of the Company, or the financial statements of the Company or any Affiliate, or of changes in Applicable Law, the Administrator, in its sole discretion, and on such terms and conditions as it deems appropriate, either by the terms of the Award or by action taken prior to the occurrence of such transaction or event and either automatically or upon the Holder's request, is hereby authorized to take any one or more of the following actions whenever the Administrator determines that such action is appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan or with respect to any Award under the Plan, to facilitate such transactions or events or to give effect to such changes in laws, regulations or principles:

(i) To provide for either (A) termination of any such Award in exchange for an amount of cash and/or other property, if any, equal to the amount that would have been attained upon the exercise of such Award or realization of the Holder's rights (and, for the avoidance of doubt, if as of the date of the occurrence of the transaction or event described in this Section 14.2 the Administrator determines in good faith that no amount would have been attained upon the exercise of such Award or realization of the Holder's rights, then such Award may be terminated by the Company without payment) or (B) the replacement of such Award with other rights or property selected by the Administrator in its sole discretion having an aggregate value not exceeding the amount that could have been attained upon the exercise of such Award or realization of the Holder's rights had such Award been currently exercisable or payable or fully vested;

(ii) To provide that such Award be assumed by the successor or survivor corporation, or a parent or subsidiary thereof, or shall be substituted for by similar options, rights or awards covering the stock of the successor or survivor corporation, or a parent or subsidiary thereof, with appropriate adjustments as to the number and kind of shares and prices;

(iii) To make adjustments in the number and type of shares of the Company's stock (or other securities or property) subject to outstanding Awards, and in the number and kind of outstanding Restricted Stock or Deferred Stock and/or in the terms and conditions of (including the grant or exercise price), and the criteria included in, outstanding Awards and Awards which may be granted in the future;

(iv) To provide that such Award shall be exercisable or payable or fully vested with respect to all shares covered thereby, notwithstanding anything to the contrary in the Plan or the applicable Program or Award Agreement; and

(v) To provide that the Award cannot vest, be exercised or become payable after such event.

(c) In connection with the occurrence of any Equity Restructuring, and notwithstanding anything to the contrary in Sections 14.2(a) and 14.2(b) hereof:

(i) The number and type of securities subject to each outstanding Award and the exercise price or grant price thereof, if applicable, shall be equitably adjusted; and/or

(ii) The Administrator shall make such equitable adjustments, if any, as the Administrator in its discretion may deem appropriate to reflect such Equity Restructuring with respect to the aggregate number and kind of shares that may be issued under the Plan (including, but not limited to, adjustments of the limitations in Section 3.1 hereof on the maximum number and kind of shares which may be issued under the Plan).

The adjustments provided under this Section 14.2(c) shall be nondiscretionary and shall be final and binding on the affected Holder and the Company.

(d) Change in Control.

(i) Notwithstanding any other provision of the Plan, in the event of a Change in Control, each outstanding Award shall be assumed or an equivalent Award substituted by the successor corporation or a parent or subsidiary of the successor corporation, in each case, as determined by the Administrator.

(ii) In the event that the successor corporation in a Change in Control and its parents and subsidiaries refuse to assume or substitute for any Award in accordance with Section 14.2(d)(i) hereof, each such non-assumed/substituted Award, except for any Performance Awards, shall become fully vested and, as applicable, exercisable and shall be deemed exercised, immediately prior to the consummation of such transaction, and all forfeiture restrictions on any or all such Awards shall lapse at such time. For the avoidance of doubt, the vesting of any Performance Awards not assumed in a Change in Control will not be automatically accelerated pursuant to this Section 14.2(d)(ii) and will instead vest pursuant to the terms and conditions of the applicable Award Agreement upon a Change in Control where the successor corporation and its parents and subsidiaries refuse to assume or substitute for any Award in accordance with Section 14.2(d)(i) hereof. If an Award vests and, as applicable, is exercised in lieu of assumption or substitution in connection with a Change in Control, the Administrator shall notify the Holder of such vesting and any applicable exercise period, and the Award shall terminate upon the Change in Control. For the avoidance of doubt, if the value of an Award that is terminated in connection with this Section 14.2(d)(ii) is zero or negative at the time of such Change in Control, such Award shall be terminated upon the Change in Control without payment of consideration therefor.

(iii) Notwithstanding anything to the contrary, in the event that, within the twelve (12) month period immediately following a Change in Control, a Holder experiences a Termination of Service by the Company for other

than Cause or by a Holder for Good Reason, then the vesting and, if applicable, exercisability of that number of Shares equal to one hundred percent (100%) of the then-unvested Shares subject to the outstanding Awards held by such Holder shall accelerate upon the date of such Termination of Service.

(e) The Administrator may, in its sole discretion, include such further provisions and limitations in any Award, agreement or certificate, as it may deem equitable and in the best interests of the Company that are not inconsistent with the provisions of the Plan.

(f) With respect to Awards which are granted to Covered Employees and are intended to qualify as Performance-Based Compensation, no adjustment or action described in this Section 14.2 or in any other provision of the Plan shall be authorized to the extent that such adjustment or action would cause such Award to fail to so qualify as Performance-Based Compensation, unless the Administrator determines that the Award should not so qualify. No adjustment or action described in this Section 14.2 or in any other provision of the Plan shall be authorized to the extent that such adjustment or action would cause the Plan to violate Section 422(b)(1) of the Code. Furthermore, no such adjustment or action shall be authorized to the extent such adjustment or action would result in short-swing profits liability under Section 16 of the Exchange Act or violate the exemptive conditions of Rule 16b-3 of the Exchange Act unless the Administrator determines that the Award is not to comply with such exemptive conditions.

(g) The existence of the Plan, the Program, the Award Agreement and the Awards granted hereunder shall not affect or restrict in any way the right or power of the Company or the stockholders of the Company to make or authorize any adjustment, recapitalization, reorganization or other change in the Company's capital structure or its business, any merger or consolidation of the Company, any issue of stock or of options, warrants or rights to purchase stock or of bonds, debentures, preferred or prior preference stocks whose rights are superior to or affect the Common Stock or the rights thereof or which are convertible into or exchangeable for Common Stock, or the dissolution or liquidation of the Company, or any sale or transfer of all or any part of its assets or business, or any other corporate act or proceeding, whether of a similar character or otherwise.

(h) In the event of any pending stock dividend, stock split, combination or exchange of shares, merger, consolidation or other distribution (other than normal cash dividends) of Company assets to stockholders, or any other change affecting the Shares or the share price of the Common Stock including any Equity Restructuring, for reasons of administrative convenience, the Company in its sole discretion may refuse to permit the exercise of any Award during a period of thirty (30) days prior to the consummation of any such transaction.

14.3 Approval of Plan by Stockholders. The Plan will be submitted for the approval of the Company's stockholders within twelve (12) months after the date of the Board's initial adoption of

the Plan. Awards may be granted or awarded prior to such stockholder approval; provided that such Awards shall not be exercisable, shall not vest and the restrictions thereon shall not lapse and no Shares shall be issued pursuant thereto prior to the time when the Plan is approved by the stockholders; and provided, further, that if such approval has not been obtained at the end of said twelve (12) month period, all Awards previously granted or awarded under the Plan shall thereupon be canceled and become null and void.

14.4 No Stockholders Rights. Except as otherwise provided herein, a Holder shall have none of the rights of a stockholder with respect to Shares covered by any Award until the Holder becomes the record owner of such Shares.

14.5 Paperless Administration. In the event that the Company establishes, for itself or using the services of a third party, an automated system for the documentation, granting or exercise of Awards, such as a system using an internet website or interactive voice response, then the paperless documentation, granting or exercise of Awards by a Holder may be permitted through the use of such an automated system.

14.6 Effect of Plan upon Other Compensation Plans. The adoption of the Plan shall not affect any other compensation or incentive plans in effect for the Company or any Affiliate. Nothing in the Plan shall be construed to limit the right of the Company or any Affiliate: (a) to establish any other forms of incentives or compensation for Employees, Directors or Consultants of the Company or any Affiliate, or (b) to grant or assume options or other rights or awards otherwise than under the Plan in connection with any proper corporate purpose including without limitation, the grant or assumption of options in connection with the acquisition by purchase, lease, merger, consolidation or otherwise, of the business, stock or assets of any corporation, partnership, limited liability company, firm or association.

14.7 Compliance with Laws. The Plan, the granting and vesting of Awards under the Plan and the issuance and delivery of Shares and the payment of money under the Plan or under Awards granted or awarded hereunder are subject to compliance with all Applicable Law, and to such approvals by any listing, regulatory or governmental authority as may, in the opinion of counsel for the Company, be necessary or advisable in connection therewith. Any securities delivered under the Plan shall be subject to such restrictions, and the person acquiring such securities shall, if requested by the Company, provide such assurances and representations to the Company as the Company may deem necessary or desirable to assure compliance with all Applicable Law. To the extent permitted by Applicable Law, the Plan and Awards granted or awarded hereunder shall be deemed amended to the extent necessary to conform to such Applicable Law.

14.8 Titles and Headings, References to Sections of the Code or Exchange Act. The titles and headings of the Sections in the Plan are for convenience of reference only and, in the event of any conflict, the text of the Plan, rather than such titles or headings, shall control. References to sections of the Code or the Exchange Act shall include any amendment or successor thereto.

14.9 Governing Law. The Plan and any agreements hereunder shall be administered, interpreted and enforced under the internal laws of the State of Delaware without regard to conflicts of laws thereof or of any other jurisdiction.

14.10 Section 409A. To the extent that the Administrator determines that any Award granted under the Plan is subject to Section 409A of the Code, the Program pursuant to which such

Award is granted and the Award Agreement evidencing such Award shall incorporate the terms and conditions required by Section 409A of the Code. To the extent applicable, the Plan, the Program and any Award Agreements shall be interpreted in accordance with Section 409A of the Code and Department of Treasury regulations and other interpretive guidance issued thereunder, including without limitation any such regulations or other guidance that may be issued after the Effective Date. Notwithstanding any provision of the Plan to the contrary, in the event that following the Effective Date the Administrator determines that any Award may be subject to Section 409A of the Code and related Department of Treasury guidance (including such Department of Treasury guidance as may be issued after the Effective Date), the Administrator may adopt such amendments to the Plan and the applicable Program and Award Agreement or adopt other policies and procedures (including amendments, policies and procedures with retroactive effect), or take any other actions, that the Administrator determines are necessary or appropriate to (a) exempt the Award from Section 409A of the Code and/or preserve the intended tax treatment of the benefits provided with respect to the Award, or (b) comply with the requirements of Section 409A of the Code and related Department of Treasury guidance and thereby avoid the application of any penalty taxes under such Section.

14.11 No Rights to Awards. No Eligible Individual or other person shall have any claim to be granted any Award pursuant to the Plan, and neither the Company nor the Administrator is obligated to treat Eligible Individuals, Holders or any other persons uniformly.

14.12 Unfunded Status of Awards. The Plan is intended to be an "unfunded" plan for incentive compensation. With respect to any payments not yet made to a Holder pursuant to an Award, nothing contained in the Plan or any Program or Award Agreement shall give the Holder any rights that are greater than those of a general creditor of the Company or any Affiliate.

14.13 Indemnification. To the extent allowable pursuant to Applicable Law, each member of the Committee or of the Board and any officer or other employee to whom authority to administer any component of the Plan is delegated shall be indemnified and held harmless by the Company from any loss, cost, liability, or expense that may be imposed upon or reasonably incurred by such member in connection with or resulting from any claim, action, suit, or proceeding to which he or she may be a party or in which he or she may be involved by reason of any action or failure to act pursuant to the Plan and against and from any and all amounts paid by him or her in satisfaction of judgment in such action, suit, or proceeding against him or her; provided he or she gives the Company an opportunity, at its own expense, to handle and defend the same before he or she undertakes to handle and defend it on his or her own behalf. The foregoing right of indemnification shall not be exclusive of any other rights of indemnification to which such persons may be entitled pursuant to the Company's Certificate of Incorporation or Bylaws, as a matter of law, or otherwise, or any power that the Company may have to indemnify them or hold them harmless.

14.14 Relationship to other Benefits. No payment pursuant to the Plan shall be taken into account in determining any benefits under any pension, retirement, savings, profit sharing, group insurance, welfare or other benefit plan of the Company or any Affiliate except to the extent otherwise expressly provided in writing in such other plan or an agreement thereunder.

14.15 Expenses. The expenses of administering the Plan shall be borne by the Company and its Affiliates.

Exhibit 10.14

ADVERUM BIOTECHNOLOGIES, INC.
2014 EQUITY INCENTIVE AWARD PLAN

STOCK OPTION GRANT NOTICE

Adverum Biotechnologies, Inc., a Delaware corporation, (the "Company"), pursuant to its 2014 Equity Incentive Award Plan, as may be amended from time to time (the "Plan"), hereby grants to the holder listed below ("Participant"), an option to purchase the number of shares of the Company's common stock ("Stock"), set forth below (the "Option"). This Option is subject to all of the terms and conditions set forth herein, as well as in the Plan and the Stock Option Agreement attached hereto as Exhibit A (the "Stock Option Agreement"), each of which are incorporated herein by reference. Unless otherwise defined herein, the terms defined in the Plan shall have the same defined meanings in this Grant Notice and the Stock Option Agreement.

Participant:	[ ]
Grant Date:	[ ]
Vesting Commencement Date:	[ ]
Exercise Price per Share:	[ ]
Total Exercise Price:	[ ]
Total Number of Shares Subject to the Option:	[ ]
Expiration Date:	[ ]
Vesting Schedule:	Subject to Participant's continued service to the Company on each of the applicable vesting dates, twenty-five percent (25%) of the total number of shares subject to the Option shall vest and become exercisable one year after the Vesting Commencement Date, and one-forty-eighth (1/48th) of the total number of shares subject to the Option shall vest and become exercisable each month thereafter, so that all of the shares subject to the Option are vested and exercisable on the fourth (4th) anniversary of the Vesting Commencement Date.

Type of Option: ☐ Incentive Stock Option[1] ☐ Non-Qualified Stock Option

[1] If this is an Incentive Stock Option, it (plus other outstanding Incentive Stock Options) cannot be first *exercisable* for more than $100,000 in value (measured by exercise price) in any calendar year. Any excess over $100,000 is a Nonstatutory Stock Option.

By his or her signature and the Company's signature below, Participant agrees to be bound by the terms and conditions of the Plan, the Stock Option Agreement, and this Grant Notice. Participant has reviewed the Stock Option Agreement, the Plan and this Grant Notice in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of this Grant Notice, the Stock Option Agreement and the Plan. Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Stock Option Agreement.

ADVERUM BIOTECHNOLOGIES, INC.:

Holder:		**PARTICIPANT:**	
By:	_____	By:	_____
Print Name:	_____	Print Name:	_____
Title:	_____		
Address:	_____	Address:	_____

EXHIBIT A
TO STOCK OPTION GRANT NOTICE

ADVERUM BIOTECHNOLOGIES, INC. STOCK OPTION AGREEMENT

Pursuant to the Stock Option Grant Notice (the "Grant Notice") to which this Stock Option Agreement (this "Agreement") is attached, Adverum Biotechnologies, Inc., a Delaware corporation (the "Company"), has granted to Participant an Option under the Company's 2014 Equity Incentive Award Plan, as may be amended from time to time (the "Plan"), to purchase the number of shares of Stock indicated in the Grant Notice.

ARTICLE 1.
GENERAL

1.1 Defined Terms. Wherever the following terms are used in this Agreement they shall have the meanings specified below, unless the context clearly indicates otherwise. Capitalized terms not specifically defined herein shall have the meanings specified in the Plan and the Grant Notice.

1.2 Incorporation of Terms of Plan. The Option is subject to the terms and conditions of the Plan which are incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan shall control.

ARTICLE 2.
GRANT OF OPTION

2.1 Grant of Option. In consideration of Participant's past and/or continued employment with or service to the Company or any Affiliate and for other good and valuable consideration, effective as of the Grant Date set forth in the Grant Notice (the "Grant Date"), the Company irrevocably grants to Participant the Option to purchase any part or all of an aggregate of the number of shares of Stock set forth in the Grant Notice, upon the terms and conditions set forth in the Plan and this Agreement, subject to adjustments as provided in Section 14.2 of the Plan. Unless designated as a Non-Qualified Stock Option in the Grant Notice, the Option shall be an Incentive Stock Option to the maximum extent permitted by law.

2.2 Exercise Price. The exercise price of the shares of Stock subject to the Option shall be as set forth in the Grant Notice, without commission or other charge; *provided*, *however*, that the price per share of the shares of Stock subject to the Option shall not be less than 100% of the Fair Market Value of a share of Stock on the Grant Date. Notwithstanding the foregoing, if this Option is designated as an Incentive Stock Option and Participant is a Greater Than 10% Stockholder as of the Date of Grant, the exercise price per share of the shares of Stock subject to the Option shall not be less than 110% of the Fair Market Value of a share of Stock on the Grant Date.

2.3 Consideration to the Company. In consideration of the grant of the Option by the Company, Participant agrees to render faithful and efficient services to the Company or any Affiliate. Nothing in the Plan or this Agreement shall confer upon Participant any right to continue in the employ or service of the Company or any Affiliate or shall interfere with or restrict in any way the rights of the Company and its Affiliates, which rights are hereby expressly reserved, to discharge or terminate the services of Participant at any time for any reason whatsoever, with or without cause, except to the extent expressly provided otherwise in a written agreement between the Company or an Affiliate and Participant.

ARTICLE 3.
PERIOD OF EXERCISABILITY

3.1 Commencement of Exercisability.

(a) Subject to Sections 3.2, 3.3, 5.11 and 5.17 hereof, the Option shall become vested and exercisable in such amounts and at such times as are set forth in the Grant Notice.

(b) No portion of the Option which has not become vested and exercisable at the date of Participant's Termination of Service shall thereafter become vested and exercisable, except as may be otherwise provided by the Administrator or as set forth in a written agreement between the Company and Participant.

(c) Notwithstanding Sections 3.1(a) hereof and the Grant Notice, but subject to Section 3.1(b) hereof, in the event of a Change in Control the Option shall be treated pursuant to Section 14.2 of the Plan.

3.2 Duration of Exercisability. The installments provided for in the vesting schedule set forth in the Grant Notice are cumulative. Each such installment which becomes vested and exercisable pursuant to the vesting schedule set forth in the Grant Notice shall remain vested and exercisable until it becomes unexercisable under Section 3.3 hereof.

3.3 Expiration of Option. The Option may not be exercised to any extent by anyone after the first to occur of the following events:

(a) The Expiration Date set forth in the Grant Notice, which shall in no event be more than ten (10) years from the Grant Date;

(b) If this Option is designated as an Incentive Stock Option and Participant, at the time the Option was granted, was a Greater Than 10% Stockholder, the expiration of five (5) years from the Grant Date;

(c) The expiration of three (3) months from the date of Participant's Termination of Service, unless such termination occurs by reason of Participant's death or disability; or

(d) The expiration of one (1) year from the date of Participant's Termination of Service by reason of Participant's death or disability.

3.4 Special Tax Consequences. Participant acknowledges that, to the extent that the aggregate Fair Market Value (determined as of the time the Option is granted) of all shares of Stock with respect to which Incentive Stock Options, including the Option (if applicable), are exercisable for the first time by Participant in any calendar year exceeds $100,000, the Option and such other options shall be Non-Qualified Stock Options to the extent necessary to comply with the limitations imposed by Section 422(d) of the Code. Participant further acknowledges that the rule set forth in the preceding sentence shall be applied by taking the Option and other "incentive stock options" into account in the order in which they were granted, as determined under Section 422(d) of the Code and the Treasury Regulations thereunder. Participant also acknowledges that an Incentive Stock Option exercised more than three (3) months after Participant's Termination of Employment, other than by reason of death or disability, will be taxed as a Non-Qualified Stock Option.

3.5 Tax Indemnity.

(a) Participant agrees to indemnify and keep indemnified the Company, any Affiliate and Participant's employing company, if different, from and against any liability for or obligation to pay any Tax Liability (a "Tax Liability" being any liability for income tax, withholding tax and any other employment related taxes or social security contributions in any jurisdiction) that is attributable to (1) the grant or exercise of, or any benefit derived by Participant from, the Option, (2) the acquisition by Participant of the Stock on exercise of the Option or (3) the disposal of any Stock.

(b) The Option cannot be exercised until Participant has made such arrangements as the Company may require for the satisfaction of any Tax Liability that may arise in connection with the exercise of the Option and/or the acquisition of the Stock by Participant. The Company shall not be required to issue, allot or transfer Stock until Participant has satisfied this obligation.

(c) Participant hereby acknowledges that the Company (i) makes no representations or undertakings regarding the treatment of any Tax Liabilities in connection with any aspect of the Option and (ii) does not commit to and is under no obligation to structure the terms of the grant or any aspect of any Award, including the Option, to reduce or eliminate Participant's liability for Tax Liabilities or achieve any particular tax result. Furthermore, if Participant becomes subject to tax in more than one jurisdiction between the date of grant of an Award, including the Option, and the date of any relevant taxable event, Participant acknowledges that the Company may be required to withhold or account for Tax Liabilities in more than one jurisdiction.

ARTICLE 4.
EXERCISE OF OPTION

4.1 Person Eligible to Exercise. Except as provided in Section 5.3 hereof, during the lifetime of Participant, only Participant may exercise the Option or any portion thereof, unless it has been disposed of pursuant to a DRO. After the death of Participant, any exercisable portion of the Option may, prior to the time when the Option becomes unexercisable under Section 3.3 hereof, be exercised by the deceased Participant's personal representative or by any person empowered to do so under the deceased Participant's will or under the then applicable laws of descent and distribution.

4.2 Partial Exercise. Any exercisable portion of the Option or the entire Option, if then wholly exercisable, may be exercised in whole or in part at any time prior to the time when the Option or portion thereof becomes unexercisable under Section 3.3 hereof. However, the Option shall not be exercisable with respect to fractional shares of Stock.

4.3 Manner of Exercise. The Option, or any exercisable portion thereof, may be exercised solely by delivery to the Secretary of the Company (or any third party administrator or other person or entity designated by the Company; for the avoidance of doubt, delivery shall include electronic delivery), during regular business hours, of all of the following prior to the time when the Option or such portion thereof becomes unexercisable under Section 3.3 hereof:

(a) An exercise notice in a form specified by the Administrator, stating that the Option or portion thereof is thereby exercised, such notice complying with all applicable rules established by the Administrator. The notice shall be signed by Participant or other person then entitled to exercise the Option or such portion of the Option;

(b) The receipt by the Company of full payment for the shares of Stock with respect to which the Option or portion thereof is exercised, including payment of any applicable withholding tax,

which shall be made by deduction from other compensation payable to Participant or in such other form of consideration permitted under Section 4.4 hereof that is acceptable to the Company;

(c) Any other written representations or documents as may be required in the Administrator's sole discretion to evidence compliance with the Securities Act, the Exchange Act or any other applicable law, rule or regulation; and

(d) In the event the Option or portion thereof shall be exercised pursuant to Section 4.1 hereof by any person or persons other than Participant, appropriate proof of the right of such person or persons to exercise the Option.

Notwithstanding any of the foregoing, the Company shall have the right to specify all conditions of the manner of exercise, which conditions may vary by country and which may be subject to change from time to time.

4.4 Method of Payment. Payment of the exercise price shall be by any of the following, or a combination thereof, at the election of Participant:

(a) Cash or check;

(b) With the consent of the Administrator, surrender of shares of Stock (including, without limitation, shares of Stock otherwise issuable upon exercise of the Option) held for such period of time as may be required by the Administrator in order to avoid adverse accounting consequences and having a Fair Market Value on the date of delivery equal to the aggregate exercise price of the Option or exercised portion thereof; or

(c) Other legal consideration acceptable to the Administrator (including, without limitation, through the delivery of a notice that Participant has placed a market sell order with a broker with respect to shares of Stock then issuable upon exercise of the Option, and that the broker has been directed to pay a sufficient portion of the net proceeds of the sale to the Company in satisfaction of the Option exercise price; *provided* that payment of such proceeds is then made to the Company at such time as may be required by the Company, but in any event not later than the settlement of such sale).

4.5 Conditions to Issuance of Stock. The shares of Stock deliverable upon the exercise of the Option, or any portion thereof, may be either previously authorized but unissued shares of Stock or issued shares of Stock which have then been reacquired by the Company. Such shares of Stock shall be fully paid and nonassessable. The Company shall not be required to issue or deliver any shares of Stock purchased upon the exercise of the Option or portion thereof prior to fulfillment of all of the conditions in Section 12.4 of the Plan and following conditions:

(a) The admission of such shares of Stock to listing on all stock exchanges on which such Stock is then listed;

(b) The completion of any registration or other qualification of such shares of Stock under any state or federal law or under rulings or regulations of the Securities and Exchange Commission or of any other governmental regulatory body, which the Administrator shall, in its absolute discretion, deem necessary or advisable;

(c) The obtaining of any approval or other clearance from any state or federal governmental agency which the Administrator shall, in its absolute discretion, determine to be necessary or advisable;

(d) The receipt by the Company of full payment for such shares of Stock, including payment of any applicable withholding tax, which may be in one or more of the forms of consideration permitted under Section 4.4 hereof; and

(e) The lapse of such reasonable period of time following the exercise of the Option as the Administrator may from time to time establish for reasons of administrative convenience.

4.6 Rights as Stockholder. The holder of the Option shall not be, nor have any of the rights or privileges of, a stockholder of the Company, including, without limitation, voting rights and rights to dividends, in respect of any shares of Stock purchasable upon the exercise of any part of the Option unless and until such shares of Stock shall have been issued by the Company and held of record by such holder (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company). No adjustment will be made for a dividend or other right for which the record date is prior to the date the shares of Stock are issued, except as provided in Section 14.2 of the Plan.

ARTICLE 5.
OTHER PROVISIONS

5.1 Administration. The Administrator shall have the power to interpret the Plan and this Agreement and to adopt such rules for the administration, interpretation and application of the Plan as are consistent therewith and to interpret, amend or revoke any such rules. All actions taken and all interpretations and determinations made by the Administrator in good faith shall be final and binding upon Participant, the Company and all other interested persons. No member of the Committee or the Board shall be personally liable for any action, determination or interpretation made in good faith with respect to the Plan, this Agreement or the Option.

5.2 Whole Shares. The Option may only be exercised for whole shares of Stock.

5.3 Option Not Transferable.

(a) Subject to Section 4.1 hereof, the Option may not be sold, pledged, assigned or transferred in any manner other than by will or the laws of descent and distribution or, subject to the consent of the Administrator, pursuant to a DRO, unless and until the Option has been exercised and the shares of Stock underlying the Option have been issued, and all restrictions applicable to such shares of Stock have lapsed. Neither the Option nor any interest or right therein shall be liable for the debts, contracts or engagements of Participant or his or her successors in interest or shall be subject to disposition by transfer, alienation, anticipation, pledge, hypothecation, encumbrance, assignment or any other means whether such disposition be voluntary or involuntary or by operation of law by judgment, levy, attachment, garnishment or any other legal or equitable proceedings (including bankruptcy) unless and until the Option has been exercised, and any attempted disposition thereof prior to exercise shall be null and void and of no effect, except to the extent that such disposition is permitted by the preceding sentence.

(b) During the lifetime of Participant, only Participant may exercise the Option (or any portion thereof), unless it has been disposed of pursuant to a DRO; after the death of Participant, any exercisable portion of the Option may, prior to the time when such portion becomes unexercisable under the Plan or this Agreement, be exercised by Participant's personal representative or by any person empowered to do so under the deceased Participant's will or under the then-applicable laws of descent and distribution.

(c) Notwithstanding any other provision in this Agreement, Participant may, in the manner determined by the Administrator, designate a beneficiary to exercise the rights of Participant and

to receive any distribution with respect to the Option upon Participant's death. A beneficiary, legal guardian, legal representative, or other person claiming any rights pursuant to the Plan is subject to all terms and conditions of the Plan and this Agreement, except to the extent the Plan and this Agreement otherwise provide, and to any additional restrictions deemed necessary or appropriate by the Administrator. If Participant is married or a domestic partner in a domestic partnership qualified under Applicable Law and resides in a community property state, a designation of a person other than Participant's spouse or domestic partner, as applicable, as his or her beneficiary with respect to more than 50% of Participant's interest in the Option shall not be effective without the prior written consent of Participant's spouse or domestic partner. If no beneficiary has been designated or survives Participant, payment shall be made to the person entitled thereto pursuant to Participant's will or the laws of descent and distribution. Subject to the foregoing, a beneficiary designation may be changed or revoked by Participant at any time provided the change or revocation is filed with the Administrator prior to Participant's death.

5.4 Tax Consultation. Participant understands that Participant may suffer adverse tax consequences as a result of the grant, vesting and/or exercise of the Option, and/or with the purchase or disposition of the shares of Stock subject to the Option. Participant represents that Participant has consulted with any tax consultants Participant deems advisable in connection with the purchase or disposition of such shares of Stock and that Participant is not relying on the Company for any tax advice.

5.5 Binding Agreement. Subject to the limitation on the transferability of the Option contained herein, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

5.6 Adjustments Upon Specified Events. The Administrator may accelerate the vesting of the Option in such circumstances as it, in its sole discretion, may determine. In addition, upon the occurrence of certain events relating to the Stock contemplated by Section 14.2 of the Plan (including, without limitation, an extraordinary cash dividend on such Stock), the Administrator shall make such adjustments the Administrator deems appropriate in the number of shares of Stock subject to the Option, the exercise price of the Option and the kind of securities that may be issued upon exercise of the Option. Participant acknowledges that the Option is subject to adjustment, modification and termination in certain events as provided in this Agreement and Section 14.2 of the Plan.

5.7 Notices. Any notice to be given under the terms of this Agreement to the Company shall be addressed to the Company in care of the Secretary of the Company at the Company's principal office, and any notice to be given to Participant shall be addressed to Participant at Participant's last address reflected on the Company's records. By a notice given pursuant to this Section 5.7, either party may hereafter designate a different address for notices to be given to that party. Any notice which is required to be given to Participant shall, if Participant is then deceased, be given to the person entitled to exercise his or her Option pursuant to Section 4.1 hereof by written notice under this Section 5.7. Any notice shall be deemed duly given when sent via email or when sent by certified mail (return receipt requested) and deposited (with postage prepaid) in a post office or branch post office regularly maintained by the United States Postal Service.

5.8 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

5.9 Governing Law. The laws of the State of Delaware shall govern the interpretation, validity, administration, enforcement and performance of the terms of this Agreement regardless of the law that might be applied under principles of conflicts of laws.

5.10 Conformity to Securities Laws. Participant acknowledges that the Plan and this Agreement are intended to conform to the extent necessary with all provisions of the Securities Act and the Exchange Act and any and all Applicable Law and regulations and rules promulgated by the Securities and Exchange Commission thereunder, and state securities laws and regulations. Notwithstanding anything herein to the contrary, the Plan shall be administered, and the Option is granted and may be exercised, only in such a manner as to conform to such Applicable Law. To the extent permitted by applicable law, the Plan and this Agreement shall be deemed amended to the extent necessary to conform to such Applicable Law.

5.11 Amendment, Suspension and Termination. To the extent permitted by the Plan, this Agreement may be wholly or partially amended or otherwise modified, suspended or terminated at any time or from time to time by the Administrator or the Board; *provided, however,* that, except as may otherwise be provided by the Plan, no amendment, modification, suspension or termination of this Agreement shall adversely affect the Option in any material way without the prior written consent of Participant.

5.12 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth in Section 5.3 hereof, this Agreement shall be binding upon Participant and his or her heirs, executors, administrators, successors and assigns.

5.13 Notification of Disposition. If this Option is designated as an Incentive Stock Option, Participant shall give prompt notice to the Company of any disposition or other transfer of any shares of Stock acquired under this Agreement if such disposition or transfer is made (a) within two (2) years from the Grant Date with respect to such shares of Stock or (b) within one (1) year after the transfer of such shares of Stock to Participant. Such notice shall specify the date of such disposition or other transfer and the amount realized, in cash, other property, assumption of indebtedness or other consideration, by Participant in such disposition or other transfer.

5.14 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if Participant is subject to Section 16 of the Exchange Act, the Plan, the Option and this Agreement shall be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3 of the Exchange Act) that are requirements for the application of such exemptive rule. To the extent permitted by applicable law, this Agreement shall be deemed amended to the extent necessary to conform to such applicable exemptive rule.

5.15 Not a Contract of Service Relationship. Nothing in this Agreement or in the Plan shall confer upon Participant any right to continue to serve as an employee or other service provider of the Company or any of its Affiliates or interfere with or restrict in any way with the right of the Company or any of its Affiliates, which rights are hereby expressly reserved, to discharge or to terminate for any reason whatsoever, with or without cause, the services of Participant's at any time.

5.16 Entire Agreement. The Plan, the Grant Notice and this Agreement (including all Exhibits thereto) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and Participant with respect to the subject matter hereof.

5.17 Section 409A. This Option is not intended to constitute "nonqualified deferred compensation" within the meaning of Section 409A of the Code (together with any Department of Treasury regulations and other interpretive guidance issued thereunder, including without limitation any

such regulations or other guidance that may be issued after the date hereof, "Section 409A"). However, notwithstanding any other provision of the Plan, the Grant Notice or this Agreement (or any Exhibits hereto), if at any time the Administrator determines that the Option (or any portion thereof) may be subject to Section 409A, the Administrator shall have the right in its sole discretion (without any obligation to do so or to indemnify Participant or any other person for failure to do so) to adopt such amendments to the Plan, the Grant Notice or this Agreement (or any Exhibits hereto), or adopt other policies and procedures (including amendments, policies and procedures with retroactive effect), or take any other actions, as the Administrator determines are necessary or appropriate either for the Option to be exempt from the application of Section 409A or to comply with the requirements of Section 409A.

5.18 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and shall not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. Participant shall have only the rights of a general unsecured creditor of the Company with respect to amounts credited and benefits payable, if any, with respect to the Option, and rights no greater than the right to receive the Stock as a general unsecured creditor with respect to options, as and when exercised pursuant to the terms hereof.

5.19 Consent to Personal Data Use. Participant acknowledges and agrees that the Company is permitted to collect, hold, store, process, modify, transfer, lock or delete certain personal (and sensitive) data in any medium about Participant (i.e., name, home address, telephone number, e-mail address, date of birth, tax identification number and payroll information) as a part of its personnel and other business records for the exclusive purpose of tracking stock option grants, processing stock option exercises and subsequent share transfers and sales, arranging for appropriate tax reporting and withholding and regulatory tracking and reporting purposes and the Company may disclose such information to third parties in the event that such disclosure is in the Company's view required for the proper tracking of stock option grants, processing stock option exercises and subsequent share transfers and sales, arranging for appropriate tax reporting and withholding and regulatory tracking. For these purposes, this personal data will be transferred to other locations, including locations outside of the European Union and in so-called insecure third-party countries that do not guarantee the data privacy protection level of the European Union.

5.20 Rules Particular To Specific Countries.

(a) Generally. Participant shall, if required by the Administrator, enter into an election with the Company or an Affiliate (in a form approved by the Company) under which any liability to the Company's (or an Affiliate's) Tax Liability, including, but not limited to, National Insurance Contributions ("NICs") and the Fringe Benefit Tax ("FBT"), is transferred to and met by Participant. For purposes of this Section 5.20, Tax Liability shall mean any and all liability under applicable non-U.S. laws, rules or regulations from any income tax, the Company's (or an Affiliate's) NICs, FBT or similar liability and Participant's NICs, FBT or similar liability that are attributable to: (A) the grant or exercise of, or any other benefit derived by Participant from the Option; (B) the acquisition by Participant of the shares of Stock on exercise of the Option; or (C) the disposal of any shares of Stock acquired upon exercise of the Option.

(b) Tax Indemnity. Participant shall indemnify and keep indemnified the Company and any of its Affiliates from and against any Tax Liability.

* * * * *

Exhibit 10.16

ADVERUM BIOTECHNOLOGIES, INC.
2014 EQUITY INCENTIVE AWARD PLAN

RESTRICTED STOCK UNIT AWARD GRANT NOTICE

Adverum Biotechnologies, Inc., a Delaware corporation, (the "Company"), pursuant to its 2014 Equity Incentive Award Plan, as amended from time to time (the "Plan"), hereby grants to the holder listed below (the "Participant"), an award of restricted stock units ("Restricted Stock Units" or "RSUs"). Each vested Restricted Stock Unit represents the right to receive, in accordance with the Restricted Stock Unit Award Agreement attached hereto as Exhibit A (the "Agreement"), one share of Common Stock ("Share"). This award of Restricted Stock Units is subject to all of the terms and conditions set forth herein and in the Agreement and the Plan, each of which are incorporated herein by reference. Unless otherwise defined herein, the terms defined in the Plan shall have the same defined meanings in this Restricted Stock Unit Award Grant Notice (the "Grant Notice") and the Agreement.

Participant:	[ ]
Grant Date:	[ ]
Total Number of RSUs:	[ ]
Vesting Commencement Date:	[ ]
Vesting Schedule:	Subject to Participant's continued service with the Company on the applicable vesting dates, twenty-five percent (25%) of the Shares subject to this award of RSUs shall vest and be released on each anniversary of the Vesting Commencement Date such that all of the Shares subject to this award of RSUs are vested and released on the fourth (4th) anniversary of the Vesting Commencement Date.
Termination:	If the Participant experiences a Termination of Service prior to the applicable vesting date, all RSUs that have not become vested on or prior to the date of such Termination of Service (after taking into consideration any vesting that may occur in connection with such Termination of Service, if any) will thereupon be automatically forfeited by the Participant without payment of any consideration therefor.

By his or her signature and the Company's signature below, the Participant agrees to be bound by the terms and conditions of the Plan, the Agreement and this Grant Notice. The Participant has reviewed the Agreement, the Plan and this Grant Notice in their entirety, has had an opportunity to obtain the advice of counsel prior to executing this Grant Notice and fully understands all provisions of this Grant Notice, the Agreement and the Plan. The Participant hereby agrees to accept as binding, conclusive and final all decisions or interpretations of the Administrator upon any questions arising under the Plan, this Grant Notice or the Agreement. In addition, by signing below, the Participant also agrees that the Company, in its sole discretion, may satisfy any withholding obligations in accordance with Section 2.6(b) of the Agreement by (i) withholding shares of Common Stock otherwise issuable to the Participant upon vesting of the RSUs, (ii) instructing a broker on the Participant's behalf to sell shares of Common Stock otherwise issuable to the Participant upon vesting of the RSUs and submit the proceeds of such sale to the Company, or (iii) using any other method permitted by Section 2.6(b) of the Agreement or the Plan.

ADVERUM BIOTECHNOLOGIES, INC.:		**PARTICIPANT:**	
By:	_____	By:	_____
Print Name:	_____	Print Name:	_____
Title:	_____		
Address:	_____	Address:	_____
	_____		_____

EXHIBIT A
TO RESTRICTED STOCK UNIT AWARD GRANT NOTICE

RESTRICTED STOCK UNIT AWARD AGREEMENT

Pursuant to the Restricted Stock Unit Award Grant Notice (the "Grant Notice") to which this Restricted Stock Unit Award Agreement (this "Agreement") is attached, Adverum Biotechnologies, Inc., a Delaware corporation (the "Company"), has granted to the Participant the number of restricted stock units ("Restricted Stock Units" or "RSUs") set forth in the Grant Notice under the Company's 2014 Equity Incentive Award Plan, as amended from time to time (the "Plan"). Each vested Restricted Stock Unit represents the right to receive one share of Common Stock ("Share"). Capitalized terms not specifically defined herein shall have the meanings specified in the Plan and Grant Notice.

ARTICLE I.

GENERAL

1.1 Incorporation of Terms of Plan. The RSUs are subject to the terms and conditions of the Plan, which are incorporated herein by reference. In the event of any inconsistency between the Plan and this Agreement, the terms of the Plan shall control.

ARTICLE II.

GRANT OF RESTRICTED STOCK UNITS

2.1 Grant of RSUs. Pursuant to the Grant Notice and upon the terms and conditions set forth in the Plan and this Agreement, effective as of the Grant Date set forth in the Grant Notice, the Company hereby grants to the Participant an award of RSUs under the Plan in consideration of the Participant's past and/or continued employment with or service to the Company or any Affiliates and for other good and valuable consideration.

2.2 Unsecured Obligation to RSUs. Unless and until the RSUs have vested in the manner set forth in Article 2 hereof, the Participant will have no right to receive Common Stock under any such RSUs. Prior to actual payment of any vested RSUs, such RSUs will represent an unsecured obligation of the Company, payable (if at all) only from the general assets of the Company.

2.3 Vesting Schedule. Subject to Section 2.5 hereof, the RSUs shall vest and become nonforfeitable with respect to the applicable portion thereof according to the vesting schedule set forth in the Grant Notice (rounding down to the nearest whole Share).

2.4 Consideration to the Company. In consideration of the grant of the award of RSUs pursuant hereto, the Participant agrees to render faithful and efficient services to the Company or any Affiliate.

2.5 Forfeiture, Termination and Cancellation Upon Termination of Service. Notwithstanding any contrary provision of this Agreement or the Plan, upon the Participant's Termination of Service for any or no reason, all Restricted Stock Units which have not vested prior to or in connection with such Termination of Service (after taking into consideration any accelerated vesting which may occur in connection with such Termination of Service (if any)) shall thereupon automatically be forfeited, terminated and cancelled as of the applicable termination date without payment of any consideration by the Company, and the Participant, or the Participant's beneficiary or personal representative, as the case may be, shall have no further rights hereunder. No portion of the RSUs which has not become vested as of the date on which the Participant incurs a Termination of Service shall thereafter become vested.

2.6 Issuance of Common Stock upon Vesting.

(a) As soon as administratively practicable following the vesting of any Restricted Stock Units pursuant to Section 2.3 hereof, but in no event later than thirty (30) days after such vesting date (for the avoidance of doubt, this deadline is intended to comply with the "short term deferral" exemption from Section 409A of the Code), the Company shall deliver to the Participant (or any transferee permitted under Section 3.2 hereof) a number of Shares (either by delivering one or more certificates for such Shares or by entering such Shares in book entry form, as determined by the Company in its sole discretion) equal to the number of RSUs subject to this Award that vest on the applicable vesting date, unless such RSUs terminate prior to the given vesting date pursuant to Section 2.5 hereof. Notwithstanding the foregoing, in the event Shares cannot be issued pursuant to Section 12.4 of the Plan, the Shares shall be issued pursuant to the preceding sentence as soon as administratively practicable after the Administrator determines that Shares can again be issued in accordance with such Section.

(b) As set forth in Section 12.2 of the Plan, the Company shall have the authority and the right to deduct or withhold, or to require the Participant to remit to the Company, an amount sufficient to satisfy all applicable federal, state and local taxes required by law to be withheld with respect to any taxable event arising in connection with the Restricted Stock Units. The Company shall not be obligated to deliver any new certificate representing Shares to the Participant or the Participant's legal representative or enter such Shares in book entry form unless and until the Participant or the Participant's legal representative shall have paid or otherwise satisfied in full the amount of all federal, state and local taxes applicable to the taxable income of the Participant resulting from the grant or vesting of the Restricted Stock Units or the issuance of Shares.

2.7 Conditions to Delivery of Shares. The Shares deliverable hereunder may be either previously authorized but unissued Shares, treasury Shares or issued Shares which have then been reacquired by the Company. Such Shares shall be fully paid and nonassessable. The Company shall not be required to issue or deliver any certificates or make any book entries evidencing Shares deliverable hereunder prior to fulfillment of the conditions set forth in Section 12.4 of the Plan.

2.8 Rights as Stockholder. The holder of the RSUs shall not be, nor have any of the rights or privileges of, a stockholder of the Company, including, without limitation, voting rights and rights to dividends, in respect of the RSUs and any Shares underlying the RSUs and deliverable hereunder unless and until such Shares shall have been issued by the Company and held of record by such holder (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company). No adjustment shall be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 14.2 of the Plan.

ARTICLE III.

OTHER PROVISIONS

3.1 Administration. The Administrator shall have the power to interpret the Plan and this Agreement and to adopt such rules for the administration, interpretation and application of the Plan as are consistent therewith and to interpret, amend or revoke any such rules. All actions taken and all interpretations and determinations made by the Administrator in good faith shall be final and binding upon the Participant, the Company and all other interested persons. No member of the Administrator or the Board shall be personally liable for any action, determination or interpretation made in good faith with respect to the Plan, this Agreement or the RSUs.

3.2 RSUs Not Transferable. The RSUs shall be subject to the restrictions on transferability set forth in Section 12.3 of the Plan; *provided, however*, that this Section 3.2 notwithstanding, with the consent of the Administrator, the RSUs may be transferred to one or more Permitted Transferees, subject to and in accordance with Section 12.3 of the Plan.

3.3 Tax Consultation. The Participant understands that the Participant may suffer adverse tax consequences in connection with the RSUs granted pursuant to this Agreement (and the Shares issuable with respect thereto). The Participant represents that the Participant has consulted with any tax consultants the Participant deems advisable in connection with the RSUs and the issuance of Shares with respect thereto and that the Participant is not relying on the Company for any tax advice.

3.4 Binding Agreement. Subject to the limitation on the transferability of the RSUs contained herein, this Agreement will be binding upon and inure to the benefit of the heirs, legatees, legal representatives, successors and assigns of the parties hereto.

3.5 Adjustments Upon Specified Events. The Administrator may accelerate the vesting of the RSUs in such circumstances as it, in its sole discretion, may determine. The Participant acknowledges that the RSUs are subject to adjustment, modification and termination in certain events as provided in this Agreement and Section 14.2 of the Plan.

3.6 Notices. Any notice to be given under the terms of this Agreement to the Company shall be addressed to the Company in care of the Secretary of the Company at the Company's principal office, and any notice to be given to the Participant shall be addressed to the Participant at the Participant's last address reflected on the Company's records. By a notice given pursuant to this Section 3.6, either party may hereafter designate a different address for notices to be given to that party. Any notice shall be deemed duly given when sent via email or when sent by certified mail (return receipt requested) and deposited (with postage prepaid) in a post office or branch post office regularly maintained by the United States Postal Service.

3.7 Participant's Representations. If the Shares issuable hereunder have not been registered under the Securities Act or any applicable state laws on an effective registration statement at the time of such issuance, the Participant shall, if required by the Company, concurrently with such issuance, make such written representations as are deemed necessary or appropriate by the Company and/or its counsel.

3.8 Titles. Titles are provided herein for convenience only and are not to serve as a basis for interpretation or construction of this Agreement.

3.9 Governing Law. The laws of the State of Delaware shall govern the interpretation, validity, administration, enforcement and performance of the terms of this Agreement regardless of the law that might be applied under principles of conflicts of laws.

3.10 Conformity to Securities Laws. The Participant acknowledges that the Plan and this Agreement are intended to conform to the extent necessary with all provisions of the Securities Act and the Exchange Act and any other Applicable Law. Notwithstanding anything herein to the contrary, the Plan shall be administered, and the RSUs are granted, only in such a manner as to conform to Applicable Law. To the extent permitted by Applicable Law, the Plan and this Agreement shall be deemed amended to the extent necessary to conform to such Applicable Law.

3.11 Amendment, Suspension and Termination. To the extent permitted by the Plan, this Agreement may be wholly or partially amended or otherwise modified, suspended or terminated at any time or from time to time by the Administrator or the Board; *provided, however,* that, except as may otherwise be provided by the Plan, no amendment, modification, suspension or termination of this Agreement shall adversely affect the RSUs in any material way without the prior written consent of the Participant.

3.12 Successors and Assigns. The Company may assign any of its rights under this Agreement to single or multiple assignees, and this Agreement shall inure to the benefit of the successors and assigns of the Company. Subject to the restrictions on transfer herein set forth in Section 3.2 hereof, this Agreement shall be binding upon the Participant and his or her heirs, executors, administrators, successors and assigns.

3.13 Limitations Applicable to Section 16 Persons. Notwithstanding any other provision of the Plan or this Agreement, if the Participant is subject to Section 16 of the Exchange Act, then the Plan, the RSUs and this Agreement shall be subject to any additional limitations set forth in any applicable exemptive rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3 of the Exchange Act) that are requirements for the application of such exemptive rule. To the extent permitted by Applicable Law, this Agreement shall be deemed amended to the extent necessary to conform to such applicable exemptive rule.

3.14 Not a Contract of Service Relationship. Nothing in this Agreement or in the Plan shall confer upon Participant any right to continue to serve as an employee or other service provider of the Company or any of its Affiliates or interfere with or restrict in any way with the right of the Company or any of its Affiliates, which rights are hereby

expressly reserved, to discharge or to terminate for any reason whatsoever, with or without cause, the services of the Participant's at any time.

3.15 Entire Agreement. The Plan, the Grant Notice and this Agreement (including all Exhibits thereto, if any) constitute the entire agreement of the parties and supersede in their entirety all prior undertakings and agreements of the Company and the Participant with respect to the subject matter hereof.

3.16 Section 409A. This Award is not intended to constitute "nonqualified deferred compensation" within the meaning of Section 409A of the Code (together with any Department of Treasury regulations and other interpretive guidance issued thereunder, including without limitation any such regulations or other guidance that may be issued after the date hereof, "Section 409A"). However, notwithstanding any other provision of the Plan, the Grant Notice or this Agreement, if at any time the Administrator determines that this Award (or any portion thereof) may be subject to Section 409A, the Administrator shall have the right in its sole discretion (without any obligation to do so or to indemnify Participant or any other person for failure to do so) to adopt such amendments to the Plan, the Grant Notice or this Agreement, or adopt other policies and procedures (including amendments, policies and procedures with retroactive effect), or take any other actions, as the Administrator determines are necessary or appropriate for this Award either to be exempt from the application of Section 409A or to comply with the requirements of Section 409A.

3.17 Limitation on Participant's Rights. Participation in the Plan confers no rights or interests other than as herein provided. This Agreement creates only a contractual obligation on the part of the Company as to amounts payable and shall not be construed as creating a trust. Neither the Plan nor any underlying program, in and of itself, has any assets. The Participant shall have only the rights of a general unsecured creditor of the Company and its Affiliates with respect to amounts credited and benefits payable, if any, with respect to the RSUs, and rights no greater than the right to receive the Common Stock as a general unsecured creditor with respect to RSUs, as and when payable hereunder.

ADVERUM BIOTECHNOLOGIES, INC.
2014 EMPLOYEE STOCK PURCHASE PLAN

ARTICLE I.
PURPOSE, SCOPE AND ADMINISTRATION OF THE PLAN

1.1 Purpose and Scope. The purpose of the Avalanche Biotechnologies, Inc. 2014 Employee Stock Purchase Plan, as it may be amended from time to time, (the "Plan") is to assist employees of Avalanche Biotechnologies, Inc., a Delaware corporation, (the "Company") and its Designated Subsidiaries in acquiring a stock ownership interest in the Company pursuant to a plan which is intended to qualify as an "employee stock purchase plan" under Section 423 of the Code and to help such employees provide for their future security and to encourage them to remain in the employment of the Company and its Subsidiaries.

ARTICLE II.
DEFINITIONS

Whenever the following terms are used in the Plan, they shall have the meaning specified below unless the context clearly indicates to the contrary. The singular pronoun shall include the plural where the context so indicates.

2.1 "Agent" means the brokerage firm, bank or other financial institution, entity or person(s), if any, engaged, retained, appointed or authorized to act as the agent of the Company or an Employee with regard to the Plan.

2.2 "Administrator" shall mean the Committee, or such individuals to which authority to administer the Plan has been delegated under Section 7.1 hereof.

2.3 "Board" shall mean the Board of Directors of the Company.

2.4 "Code" shall mean the Internal Revenue Code of 1986, as amended.

2.5 "Committee" shall mean the Compensation Committee of the Board.

2.6 "Common Stock" shall mean the common stock of the Company.

2.7 "Company" shall have such meaning as set forth in Section 1.1 hereof.

2.8 "Compensation" of an Employee shall mean the regular straight-time earnings or base salary, bonuses and commissions paid to the Employee from the Company on each Payday as compensation for services to the Company or any Designated Subsidiary, before deduction for any salary deferral contributions made by the Employee to any tax-qualified or nonqualified deferred compensation plan, including overtime, shift differentials, vacation pay, salaried production schedule premiums, holiday pay, jury duty pay, funeral leave pay, paid time off, military pay, prior week adjustments and weekly bonus, but excluding education or tuition reimbursements, imputed income arising under any group insurance or benefit program, travel

expenses, business and moving reimbursements, income received in connection with any stock options, restricted stock, restricted stock units or other compensatory equity awards and all contributions made by the Company or any Designated Subsidiary for the Employee's benefit under any employee benefit plan now or hereafter established. Such Compensation shall be calculated before deduction of any income or employment tax withholdings, but shall be withheld from the Employee's net income.

2.9 "Designated Subsidiary" shall mean each Subsidiary that have been designated by the Board or Committee from time to time in its sole discretion as eligible to participate in the Plan, including any Subsidiary in existence on the Effective Date and any Subsidiary formed or acquired following the Effective Date, in accordance with Section 7.2 hereof.

2.10 "Effective Date" shall mean the date immediately preceding the date the Company's registration statement relating to its initial public offering becomes effective, provided that the Board has adopted and the Company's stockholders have approved the Plan prior to or on such date.

2.11 "Eligible Employee" shall mean an Employee who (a) is customarily scheduled to work at least twenty (20) hours per week, (b) whose customary employment is more than five (5) months in a calendar year and (c) after the granting of the Option would not be deemed for purposes of Section 423(b)(3) of the Code to possess five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or any Subsidiary. For purposes of clause (c), the rules of Section 424(d) of the Code with regard to the attribution of stock ownership shall apply in determining the stock ownership of an individual, and stock which an Employee may purchase under outstanding options shall be treated as stock owned by the Employee. Notwithstanding the foregoing, the Administrator may exclude from participation in the Plan as an Eligible Employee (x) any Employee that is a "highly compensated employee" of the Company or any Designated Subsidiary (within the meaning of Section 414(q) of the Code), or that is such a "highly compensated employee" (A) with compensation above a specified level, (B) who is an officer and/or (C) is subject to the disclosure requirements of Section 16(a) of the Exchange Act and/or (y) any Employee who is a citizen or resident of a foreign jurisdiction (without regard to whether they are also a citizen of the United States or a resident alien (within the meaning of Section 7701(b)(1)(A) of the Code)) if either (i) the grant of the Option is prohibited under the laws of the jurisdiction governing such Employee, or (ii) compliance with the laws of the foreign jurisdiction would cause the Plan or the Option to violate the requirements of Section 423 of the Code; provided that any exclusion in clauses (x), and/or (y) shall be applied in an identical manner under each Offering Period to all Employees of the Company and all Designated Subsidiaries, in accordance with Treasury Regulation Section 1.423-2(e).

2.12 "Employee" shall mean any person who renders services to the Company or a Designated Subsidiary in the status of an employee within the meaning of Section 3401(c) of the Code. "Employee" shall not include any director of the Company or a Designated Subsidiary who does not render services to the Company or a Designated Subsidiary in the status of an employee within the meaning of Section 3401(c) of the Code. For purposes of the Plan, the

employment relationship shall be treated as continuing intact while the individual is on military leave, sick leave or other leave of absence approved by the Company or Designated Subsidiary and meeting the requirements of Treasury Regulation Section 1.421-1(h)(2). Where the period of leave exceeds three (3) months, or such other period specified in Treasury Regulation Section 1.421-1(h)(2), and the individual's right to reemployment is not guaranteed either by statute or by contract, the employment relationship shall be deemed to have terminated on the first day immediately following such three (3)-month period, or such other period specified in Treasury Regulation Section 1.421-1(h)(2).

2.13 "Enrollment Date" shall mean the first date of each Offering Period.

2.14 "Exercise Date" shall mean the last Trading Day of each Offering Period, except as provided in Section 5.2 hereof.
2.15 "Exchange Act" shall mean the Securities Exchange Act of 1934, as amended.

2.16 "Fair Market Value" shall mean, as of any date, the value of Common Stock determined as follows:

(a) If the Common Stock is (i) listed on any established securities exchange (such as the New York Stock Exchange, the NASDAQ Global Market and the NASDAQ Global Select Market), (ii) listed on any national market system or (iii) listed, quoted or traded on any automated quotation system, its Fair Market Value shall be the closing sales price for a share of Common Stock as quoted on such exchange or system for such date or, if there is no closing sales price for a share of Common Stock on the date in question, the closing sales price for a share of Stock on the last preceding date for which such quotation exists, as reported in The Wall Street Journal or such other source as the Administrator deems reliable;

(b) If the Common Stock is not listed on an established securities exchange, national market system or automated quotation system, but the Common Stock is regularly quoted by a recognized securities dealer, its Fair Market Value shall be the mean of the high bid and low asked prices for such date or, if there are no high bid and low asked prices for a share of Common Stock on such date, the high bid and low asked prices for a share of Common Stock on the last preceding date for which such information exists, as reported in The Wall Street Journal or such other source as the Administrator deems reliable; or

(c) If the Common Stock is neither listed on an established securities exchange, national market system or automated quotation system nor regularly quoted by a recognized securities dealer, its Fair Market Value shall be established by the Administrator in good faith.

2.17 "Grant Date" shall mean the first Trading Day of an Offering Period.

2.18 "New Exercise Date" shall have such meaning as set forth in Section 5.2(b) hereof.

2.19 "Offering Period" shall mean such period of time, which shall be determined by the Committee, with respect to which Options are granted to Participants. The duration and timing of Offering Periods may be changed by the Board or Committee, in its sole discretion. In no event may an Offering Period exceed twenty-seven (27) months.

2.20 "Option" shall mean the right to purchase shares of Common Stock pursuant to the Plan during each Offering Period.

2.21 "Option Price" shall mean the purchase price of a share of Common Stock hereunder as provided in Section 4.2 hereof.

2.22 "Parent" means any entity that is a parent corporation of the Company within the meaning of Section 424 of the Code and the Treasury Regulations thereunder.

2.23 "Participant" shall mean any Eligible Employee who elects to participate in the Plan.

2.24 "Payday" shall mean the regular and recurring established day for payment of Compensation to an Employee of the Company or any Designated Subsidiary.

2.25 "Plan" shall have such meaning as set forth in Section 1.1 hereof.

2.26 "Plan Account" shall mean a bookkeeping account established and maintained by the Company in the name of each Participant.

2.27 "Section 423 Option" shall have such meaning as set forth in Section 3.1(b) hereof.

2.28 "Subsidiary" shall mean any entity that is a subsidiary corporation of the Company within the meaning of Section 424 of the Code and the Treasury Regulations thereunder. In addition, with respect to any sub-plans adopted under Section 7.1(d) hereof which are designed to be outside the scope of Section 423 of the Code, Subsidiary shall include any corporate or noncorporate entity in which the Company has a direct or indirect equity interest or significant business relationship.

2.29 "Trading Day" shall mean a day on which the principal securities exchange on which the Common Stock is listed is open for trading or, if the Common Stock is not listed on a securities exchange, shall mean a business day, as determined by the Administrator in good faith.

2.30 "Withdrawal Election" shall have such meaning as set forth in Section 6.1(a) hereof.

ARTICLE III.
PARTICIPATION

3.1 Eligibility.

(a) Any Eligible Employee who shall be employed by the Company or a Designated Subsidiary on a given Enrollment Date for an Offering Period shall be eligible to participate in the Plan during such Offering Period, subject to the requirements of Articles IV and V hereof, and the limitations imposed by Section 423(b) of the Code and the Treasury Regulations thereunder.

(b) No Eligible Employee shall be granted an Option under the Plan which permits the Participant's rights to purchase shares of Common Stock under the Plan, and to purchase stock under all other employee stock purchase plans of the Company, any Parent or any Subsidiary subject to the Section 423 of the Code (any such Option or other option, a "Section 423 Option"), to accrue at a rate which exceeds $25,000 of fair market value of such stock (determined at the time the Section 423 Option is granted) for each calendar year in which any Section 423 Option granted to the Participant is outstanding at any time. For purposes of the limitation imposed by this subsection,

(i) the right to purchase stock under a Section 423 Option accrues when the Section 423 Option (or any portion thereof) first becomes exercisable during the calendar year,

(ii) the right to purchase stock under a Section 423 Option accrues at the rate provided in the Section 423 Option, but in no case may such rate exceed $25,000 of fair market value of such stock (determined at the time such option is granted) for any one calendar year, and

(iii) a right to purchase stock which has accrued under a Section 423 Option may not be carried over to any other Section 423 Option; provided that Participants may carry forward amounts so accrued that represent a fractional share of stock and were withheld but not applied towards the purchase of Common Stock under an earlier Offering Period, and may apply such amounts towards the purchase of additional shares of Common Stock under a subsequent Offering Period.

The limitation under this Section 3.1(b) shall be applied in accordance with Section 423(b)(8) of the Code and the Treasury Regulations thereunder.

3.2 Election to Participate; Payroll Deductions.

(a) Except as provided in Section 3.3 hereof, an Eligible Employee may become a Participant in the Plan only by means of payroll deduction. Each individual who is an Eligible Employee as of an Offering Period's Enrollment Date may elect to participate in such Offering Period and the Plan by delivering to the Company a payroll deduction authorization no later such period of time prior to the applicable Enrollment Date as determined by the Administrator, in its sole discretion.

(b) Subject to Section 3.1(b) hereof, payroll deductions (i) shall be equal to at least one percent (1%) of the Participant's Compensation as of each Payday of the Offering Period following the Enrollment Date, but not more than the lesser of fifteen percent (15%) of the Participant's Compensation as of each Payday of the Offering Period following the Enrollment Date or $25,000 per Offering Period; and (ii) may be expressed either as (A) a whole number percentage, or (B) a fixed dollar amount. Amounts deducted from a Participant's Compensation with respect to an Offering Period

pursuant to this Section 3.2 shall be deducted each Payday through payroll deduction and credited to the Participant's Plan Account.

(c) Following at least one (1) payroll deduction, a Participant may decrease (to as low as zero) the amount deducted from such Participant's Compensation only once during an Offering Period upon ten (10) calendar days' prior written notice to the Company. A Participant may not increase the amount deducted from such Participant's Compensation during an Offering Period.

(d) Notwithstanding the foregoing, upon the termination of an Offering Period, each Participant in such Offering Period shall automatically participate in the immediately following Offering Period at the same payroll deduction percentage or fixed amount as in effect at the termination of the prior Offering Period, unless such Participant delivers to the Company a different election with respect to the successive Offering Period in accordance with Section 3.1(a) hereof, or unless such Participant becomes ineligible for participation in the Plan.

3.3 Leave of Absence. During leaves of absence approved by the Company meeting the requirements of Treasury Regulation Section 1.421-1(h)(2) under the Code, a Participant may continue participation in the Plan by making cash payments to the Company on his or her normal payday equal to his or her authorized payroll deduction.

ARTICLE IV.
PURCHASE OF SHARES

4.1 Grant of Option. Each Participant shall be granted an Option with respect to an Offering Period on the applicable Grant Date. Subject to the limitations of Section 3.1(b) hereof, the number of shares of Common Stock subject to a Participant's Option shall be determined by dividing (a) such Participant's payroll deductions accumulated prior to such Exercise Date and retained in the Participant's Plan Account on such Exercise Date by (b) the applicable Option Price; provided that in no event shall a Participant be permitted to purchase during each Offering Period more than 3,000 shares of Common Stock (subject to any adjustment pursuant to Section 5.2 hereof). The Administrator may, for future Offering Periods, increase or decrease, in its absolute discretion, the maximum number of shares of Common Stock that a Participant may purchase during such future Offering Periods. Each Option shall expire on the Exercise Date for the applicable Offering Period immediately after the automatic exercise of the Option in accordance with Section 4.3 hereof, unless such Option terminates earlier in accordance with Article 6 hereof.

4.2 Option Price. The "Option Price" per share of Common Stock to be paid by a Participant upon exercise of the Participant's Option on the applicable Exercise Date for an Offering Period shall be equal to eighty five percent (85%) of the lesser of the Fair Market Value of a share of Common Stock on (a) the applicable Grant Date and (b) the applicable Exercise Date; provided that in no event shall the Option Price per share of Common Stock be less than the par value per share of the Common Stock.

4.3 Purchase of Shares.

(a) On the applicable Exercise Date for an Offering Period, each Participant shall automatically and without any action on such Participant's part be deemed to have exercised his or her Option to purchase at the applicable per share Option Price the largest number of whole shares of Common Stock which can be purchased with the amount in the Participant's Plan Account. Any balance less than the per share Option Price that is remaining in the Participant's Plan Account (after exercise of such Participant's Option) as of the Exercise Date shall be carried forward to the next Offering Period, unless the Participant has elected to withdraw from the Plan pursuant to Section 6.1 hereof or, pursuant to Section 6.2 hereof, such Participant has ceased to be an Eligible Employee. Any balance not carried forward to the next Offering Period in accordance with the prior sentence promptly shall be refunded to the applicable Participant. For the avoidance of doubt, in no event shall an amount greater than or equal to the per share Option Price as of an Exercise Date be carried forward to the next Offering Period.

(b) As soon as practicable following the applicable Exercise Date, the number of shares of Common Stock purchased by such Participant pursuant to Section 4.3(a) hereof shall be delivered (either in share certificate or book entry form), in the Company's sole discretion, to either (i) the Participant or (ii) an account established in the Participant's name at a stock brokerage or other financial services firm designated by the Company. If the Company is required to obtain from any commission or agency authority to issue any such shares of Common Stock, the Company shall seek to obtain such authority. Inability of the Company to obtain from any such commission or agency authority which counsel for the Company deems necessary for the lawful issuance of any such shares shall relieve the Company from liability to any Participant except to refund to the Participant such Participant's Plan Account balance, without interest thereon.

4.4 Transferability of Rights.

(a) An Option granted under the Plan shall not be transferable, other than by will or the applicable laws of descent and distribution, and is exercisable during the Participant's lifetime only by the Participant. No option or interest or right to the Option shall be available to pay off any debts, contracts or engagements of the Participant or his or her successors in interest or shall be subject to disposition by pledge, encumbrance, assignment or any other means whether such disposition be voluntary or involuntary or by operation of law by judgment, levy, attachment, garnishment or any other legal or equitable proceedings (including bankruptcy), and any attempt at disposition of the option shall have no effect.

ARTICLE V.
PROVISIONS RELATING TO COMMON STOCK

5.1 Common Stock Reserved. Subject to adjustment as provided in Section 5.2 hereof, the maximum number of shares of Common Stock that shall be made available for sale under the

Plan shall be the sum of (a) 208,833 shares of Common Stock and (b) an annual increase on the first day of each year beginning in 2015 and ending in 2024, in each case subject to the approval of the Administrator on or prior to the applicable date, equal to the lesser of (i) one percent (1%) of the shares of Common Stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (ii) such number of shares of Common Stock as determined by the Board; provided, however, no more than 3,000,000 shares of Common Stock may be issued under the Plan. Shares of Common Stock made available for sale under the Plan may be authorized but unissued shares, treasury shares of Common Stock, or reacquired shares reserved for issuance under the Plan.

5.2 Adjustments Upon Changes in Capitalization, Dissolution, Liquidation, Merger or Asset Sale.

(a) Changes in Capitalization. Subject to any required action by the stockholders of the Company, the number of shares of Common Stock which have been authorized for issuance under the Plan but not yet placed under Option, as well as the price per share and the number of shares of Common Stock covered by each Option under the Plan which has not yet been exercised shall be proportionately adjusted for any increase or decrease in the number of issued shares of Common Stock resulting from a stock split, reverse stock split, stock dividend, combination or reclassification of the Common Stock, or any other increase or decrease in the number of shares of Common Stock effected without receipt of consideration by the Company; provided, however, that conversion of any convertible securities of the Company shall not be deemed to have been "effected without receipt of consideration." Such adjustment shall be made by the Administrator, whose determination in that respect shall be final, binding and conclusive. Except as expressly provided herein, no issuance by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of shares of Common Stock subject to an Option.

(b) Dissolution or Liquidation. In the event of the proposed dissolution or liquidation of the Company, the Offering Period then in progress shall be shortened by setting a new Exercise Date (the "New Exercise Date"), and shall terminate immediately prior to the consummation of such proposed dissolution or liquidation, unless provided otherwise by the Administrator. The New Exercise Date shall be before the date of the Company's proposed dissolution or liquidation. The Administrator shall notify each Participant in writing, at least ten (10) business days prior to the New Exercise Date, that the Exercise Date for the Participant's Option has been changed to the New Exercise Date and that the Participant's Option shall be exercised automatically on the New Exercise Date, unless prior to such date the Participant has withdrawn from the Offering Period as provided in Section 6.1 hereof.

(c) Merger or Asset Sale. In the event of a proposed sale of all or substantially all of the assets of the Company, or the merger of the Company with or into another corporation, each outstanding Option shall be assumed or an equivalent Option

substituted by the successor corporation or a Parent or Subsidiary of the successor corporation. In the event that the successor corporation refuses to assume or substitute for the Option, any Offering Periods then in progress shall be shortened by setting a New Exercise Date and any Offering Periods then in progress shall end on the New Exercise Date. The New Exercise Date shall be before the date of the Company's proposed sale or merger. The Administrator shall notify each Participant in writing, at least ten (10) business days prior to the New Exercise Date, that the Exercise Date for the Participant's Option has been changed to the New Exercise Date and that the Participant's Option shall be exercised automatically on the New Exercise Date, unless prior to such date the Participant has withdrawn from the Offering Period as provided in Section 6.1 hereof.

5.3 Insufficient Shares. If the Administrator determines that, on a given Exercise Date, the number of shares of Common Stock with respect to which Options are to be exercised may exceed the number of shares of Common Stock remaining available for sale under the Plan on such Exercise Date, the Administrator shall make a pro rata allocation of the shares of Common Stock available for issuance on such Exercise Date in as uniform a manner as shall be practicable and as it shall determine in its sole discretion to be equitable among all Participants exercising Options to purchase Common Stock on such Exercise Date, and unless additional shares are authorized for issuance under the Plan, no further Offering Periods shall take place and the Plan shall terminate pursuant to Section 7.5 hereof. If an Offering Period is so terminated, then the balance of the amount credited to the Participant's Plan Account which has not been applied to the purchase of shares of Common Stock shall be paid to such Participant in one lump sum in cash within thirty (30) days after such Exercise Date, without any interest thereon.

5.4 Rights as Stockholders. With respect to shares of Common Stock subject to an Option, a Participant shall not be deemed to be a stockholder of the Company and shall not have any of the rights or privileges of a stockholder. A Participant shall have the rights and privileges of a stockholder of the Company when, but not until, shares of Common Stock have been deposited in the designated brokerage account following exercise of his or her Option.

ARTICLE VI.
TERMINATION OF PARTICIPATION

6.1 Cessation of Contributions; Voluntary Withdrawal.

(a) A Participant may cease payroll deductions during an Offering Period and elect to withdraw from the Plan by delivering written notice of such election to the Company in such form and at such time prior to the Exercise Date for such Offering Period as may be established by the Administrator (a "Withdrawal Election"). A Participant electing to withdraw from the Plan may elect to either (i) withdraw all of the funds then credited to the Participant's Plan Account as of the date on which the Withdrawal Election is received by the Company, in which case amounts credited to such Plan Account shall be returned to the Participant in one (1) lump-sum payment in cash within thirty (30) days after such election is received by the Company, without any interest thereon, and the Participant shall cease to participate in the Plan and the

Participant's Option for such Offering Period shall terminate; or (ii) exercise the Option for the maximum number of whole shares of Common Stock on the applicable Exercise Date with any remaining Plan Account balance returned to the Participant in one (1) lump-sum payment in cash within thirty (30) days after such Exercise Date, without any interest thereon, and after such exercise cease to participate in the Plan. Upon receipt of a Withdrawal Election, the Participant's payroll deduction authorization and his or her Option to purchase under the Plan shall terminate.

(b) A participant's withdrawal from the Plan shall not have any effect upon his or her eligibility to participate in any similar plan which may hereafter be adopted by the Company or in succeeding Offering Periods which commence after the termination of the Offering Period from which the Participant withdraws.

(c) A Participant who ceases contributions to the Plan during any Offering Period shall not be permitted to resume contributions to the Plan during that Offering Period.

6.2 Termination of Eligibility. Upon a Participant's ceasing to be an Eligible Employee, for any reason, such Participant's Option for the applicable Offering Period shall automatically terminate, he or she shall be deemed to have elected to withdraw from the Plan, and such Participant's Plan Account shall be paid to such Participant or, in the case of his or her death, to the person or persons entitled thereto pursuant to applicable law, within thirty (30) days after such cessation of being an Eligible Employee, without any interest thereon.

ARTICLE VII.
GENERAL PROVISIONS

7.1 Administration.

(a) The Plan shall be administered by the Committee, which shall be composed of members of the Board. The Committee may delegate administrative tasks under the Plan to the services of an Agent and/or Employees to assist in the administration of the Plan, including establishing and maintaining an individual securities account under the Plan for each Participant.

(b) It shall be the duty of the Administrator to conduct the general administration of the Plan in accordance with the provisions of the Plan. The Administrator shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To establish Offering Periods;

(ii) To determine when and how Options shall be granted and the provisions and terms of each Offering Period (which need not be identical);

(iii) To select Designated Subsidiaries in accordance with Section 7.2 hereof; and

(iv) To construe and interpret the Plan, the terms of any Offering Period and the terms of the Options and to adopt such rules for the administration,

interpretation, and application of the Plan as are consistent therewith and to interpret, amend or revoke any such rules. The Administrator, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan, any Offering Period or any Option, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effect, subject to Section 423 of the Code and the Treasury Regulations thereunder.

(c) The Administrator may adopt rules or procedures relating to the operation and administration of the Plan to accommodate the specific requirements of local laws and procedures. Without limiting the generality of the foregoing, the Administrator is specifically authorized to adopt rules and procedures regarding handling of participation elections, payroll deductions, payment of interest, conversion of local currency, payroll tax, withholding procedures and handling of stock certificates which vary with local requirements. In its absolute discretion, the Board may at any time and from time to time exercise any and all rights and duties of the Administrator under the Plan.

(d) The Administrator may adopt sub-plans applicable to particular Designated Subsidiaries or locations, which sub-plans may be designed to be outside the scope of Section 423 of the Code. The rules of such sub-plans may take precedence over other provisions of this Plan, with the exception of Section 5.1 hereof, but unless otherwise superseded by the terms of such sub-plan, the provisions of this Plan shall govern the operation of such sub-plan.

(e) All expenses and liabilities incurred by the Administrator in connection with the administration of the Plan shall be borne by the Company. The Administrator may, with the approval of the Committee, employ attorneys, consultants, accountants, appraisers, brokers or other persons. The Administrator, the Company and its officers and directors shall be entitled to rely upon the advice, opinions or valuations of any such persons. All actions taken and all interpretations and determinations made by the Administrator in good faith shall be final and binding upon all Participants, the Company and all other interested persons. No member of the Board or Administrator shall be personally liable for any action, determination or interpretation made in good faith with respect to the Plan or the options, and all members of the Board or Administrator shall be fully protected by the Company in respect to any such action, determination, or interpretation.

7.2 Designation of Subsidiary Corporations. The Board or Committee shall designate from among the Subsidiaries, as determined from time to time, the Subsidiary or Subsidiaries that shall constitute Designated Subsidiaries. The Board or Committee may designate a Subsidiary, or terminate the designation of a Subsidiary, without the approval of the stockholders of the Company.

7.3 Reports. Individual accounts shall be maintained for each Participant in the Plan. Statements of Plan Accounts shall be given to Participants at least annually, which statements shall set forth the amounts of payroll deductions, the Option Price, the number of shares purchased and the remaining cash balance, if any.

7.4 No Right to Employment. Nothing in the Plan shall be construed to give any person (including any Participant) the right to remain in the employ of the Company, a Parent or a Subsidiary or to affect the right of the Company, any Parent or any Subsidiary to terminate the employment of any person (including any Participant) at any time, with or without cause, which right is expressly reserved.

7.5 Amendment and Termination of the Plan.

(a) The Board may, in its sole discretion, amend, suspend or terminate the Plan at any time and from time to time; provided, however, that without approval of the Company's stockholders given within twelve (12) months before or after action by the Board, the Plan may not be amended to increase the maximum number of shares of Common Stock subject to the Plan or change the designation or class of Eligible Employees; and provided, further that without approval of the Company's stockholders, the Plan may not be amended in any manner that would cause the Plan to no longer be an "employee stock purchase plan" within the meaning of Section 423(b) of the Code.

(b) In the event the Administrator determines that the ongoing operation of the Plan may result in unfavorable financial accounting consequences, the Administrator may, to the extent permitted under Section 423 of the Code, in its discretion and, to the extent necessary or desirable, modify or amend the Plan to reduce or eliminate such accounting consequence including, but not limited to:

(i) altering the Option Price for any Offering Period including an Offering Period underway at the time of the change in Option Price;

(ii) shortening any Offering Period so that the Offering Period ends on a new Exercise Date, including an Offering Period underway at the time of the Administrator action; and

(iii) allocating shares of Common Stock.

Such modifications or amendments shall not require stockholder approval or consent of any Participant.

(c) Upon termination of the Plan, the balance in each Participant's Plan Account shall be refunded as soon as practicable after such termination, without any interest thereon.

7.6 Use of Funds; No Interest Paid. All funds received by the Company by reason of purchase of Common Stock under the Plan shall be included in the general funds of the Company free of any trust or other restriction and may be used for any corporate purpose. No interest shall be paid to any Participant or credited under the Plan.

7.7 Term; Approval by Stockholders. No Option may be granted during any period of suspension of the Plan or after termination of the Plan. The Plan shall be submitted for the approval of the Company's stockholders within twelve (12) months after the date of the Board's initial adoption of the Plan. Options may be granted prior to such stockholder approval;

provided, however, that such Options shall not be exercisable prior to the time when the Plan is approved by the stockholders; provided, further that if such approval has not been obtained by the end of said twelve (12)-month period, all Options previously granted under the Plan shall thereupon terminate and be canceled and become null and void without being exercised.

7.8 Effect Upon Other Plans. The adoption of the Plan shall not affect any other compensation or incentive plans in effect for the Company, any Parent or any Subsidiary. Nothing in the Plan shall be construed to limit the right of the Company, any Parent or any Subsidiary (a) to establish any other forms of incentives or compensation for Employees of the Company or any Parent or any Subsidiary, or (b) to grant or assume Options otherwise than under the Plan in connection with any proper corporate purpose, including, but not by way of limitation, the grant or assumption of options in connection with the acquisition, by purchase, lease, merger, consolidation or otherwise, of the business, stock or assets of any corporation, firm or association.

7.9 Conformity to Securities Laws. Notwithstanding any other provision of the Plan, the Plan and the participation in the Plan by any individual who is then subject to Section 16 of the Exchange Act shall be subject to any additional limitations set forth in any applicable exemption rule under Section 16 of the Exchange Act (including any amendment to Rule 16b-3 of the Exchange Act) that are requirements for the application of such exemptive rule. To the extent permitted by applicable law, the Plan shall be deemed amended to the extent necessary to conform to such applicable exemptive rule.

7.10 Notice of Disposition of Shares. Each Participant shall give the Company prompt notice of any disposition or other transfer of any shares of Common Stock, acquired pursuant to the exercise of an Option, if such disposition or transfer is made (a) within two (2) years after the applicable Grant Date or (b) within one (1) year after the transfer of such shares of Common Stock to such Participant upon exercise of such Option. The Company may direct that any certificates evidencing shares acquired pursuant to the Plan refer to such requirement.

7.11 Tax Withholding. The Company or any Parent or any Subsidiary shall be entitled to require payment in cash or deduction from other compensation payable to each Participant of any sums required by federal, state or local tax law to be withheld with respect to any purchase of shares of Common Stock under the Plan or any sale of such shares.

7.12 Governing Law. The Plan and all rights and obligations thereunder shall be construed and enforced in accordance with the laws of the State of Delaware.

7.13 Notices. All notices or other communications by a participant to the Company under or in connection with the Plan shall be deemed to have been duly given when received in the form specified by the Company at the location, or by the person, designated by the Company for the receipt thereof.

7.14 Conditions To Issuance of Shares.

(a) Notwithstanding anything herein to the contrary, the Company shall not be required to issue or deliver any certificates or make any book entries evidencing shares of

Common Stock pursuant to the exercise of an Option by a Participant, unless and until the Board or the Committee has determined, with advice of counsel, that the issuance of such shares of Common Stock is in compliance with all applicable laws, regulations of governmental authorities and, if applicable, the requirements of any securities exchange or automated quotation system on which the shares of Common Stock are listed or traded, and the shares of Common Stock are covered by an effective registration statement or applicable exemption from registration. In addition to the terms and conditions provided herein, the Board or the Committee may require that a Participant make such reasonable covenants, agreements, and representations as the Board or the Committee, in its discretion, deems advisable in order to comply with any such laws, regulations, or requirements.

(b) All certificates for shares of Common Stock delivered pursuant to the Plan and all shares of Common Stock issued pursuant to book entry procedures are subject to any stop-transfer orders and other restrictions as the Committee deems necessary or advisable to comply with federal, state, or foreign securities or other laws, rules and regulations and the rules of any securities exchange or automated quotation system on which the shares of Common Stock are listed, quoted, or traded. The Committee may place legends on any certificate or book entry evidencing shares of Common Stock to reference restrictions applicable to the shares of Common Stock.

(c) The Committee shall have the right to require any Participant to comply with any timing or other restrictions with respect to the settlement, distribution or exercise of any Option, including a window-period limitation, as may be imposed in the sole discretion of the Committee.

(d) Notwithstanding any other provision of the Plan, unless otherwise determined by the Committee or required by any applicable law, rule or regulation, the Company may, in lieu of delivering to any Participant certificates evidencing shares of Common Stock issued in connection with any Option, record the issuance of shares of Common Stock in the books of the Company (or, as applicable, its transfer agent or stock plan administrator).

7.15 Equal Rights and Privileges. Except with respect to sub-plans designed to be outside the scope of Section 423 of the Code, all Eligible Employees of the Company (or of any Designated Subsidiary) shall have equal rights and privileges under this Plan to the extent required under Section 423 of the Code or the regulations promulgated thereunder so that this Plan qualifies as an "employee stock purchase plan" within the meaning of Section 423 of the Code or the Treasury Regulations thereunder. Any provision of this Plan that is inconsistent with Section 423 of the Code or the Treasury Regulations thereunder shall, without further act or amendment by the Company or the Board, be reformed to comply with the equal rights and privileges requirement of Section 423 of the Code or the Treasury Regulations thereunder.

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Exhibit 10.30

5/4/2015

Jennifer Cheng 100 42°d Avenue

San Mateo, CA 94403

Re: Employment Terms for Sr. Patent Counsel/Director IP

Dear Ms. Cheng:

This letter agreement (the "Agreement") memorializes the employment terms for your anticipated hire by Avalanche Biotechnologies, Inc. (the "Company") in the position of Sr. **Patent Counsel/ Director IP** reporting to Hans Hull, SVP Business Operations. These terms will become effective on June 2, 2015 or at such later date by mutual agreement and as approved by the Board of Directors of the Company (as applicable, the "Hire Date").

Effective as of the Hire Date, your employment terms will be as follows:

1. Compensation and Benefits.

Your base salary will be $214,000.00 per annum, subject to payroll deductions and all required withholdings, representing full-time employment with the Company. Your salary will be paid in accordance with the Company's standard payroll schedule.

You will receive a one-time signing bonus of $20,000.00. Should you terminate your employment for any reason, or should the Company terminate your employment for Cause, within twelve (12) months of the Hire Date, you will be responsible for repaying 100% of the one-time signing bonus.

In addition, for the calendar year starting 2015 you will be eligible to earn an annual performance bonus with a target bonus amount equal to Twenty Percent (20%) ***("Target Percentage")*** of your salary earned during the bonus year, provided that you are actively employed from the Hire Date through and including the date of bonus grants. Your annual bonus will be calculated based on attainment of individual goals (including corporate and personal objectives) to be determined by the Company's management each year. Bonus payments will be in the form of cash and/or incentive stock options, and will be granted entirely at the discretion of the Company's CEO and Board of Directors. Any cash bonus payments will be less payroll deductions and all required withholdings.

You will be eligible to participate in the Company's general employee benefits in accordance with the terms, conditions and limitations of the benefit plans to the extent such plans have been established by the Company.

2. Incentive Stock Option grant.

In addition to the compensation and benefits described above, the Company will grant you, subject to the approval of the Company's board of directors, the option to purchase 15,000 shares of the Company's common stock, at the fair market value as determined by the Company's board of directors at the date of the grant. The foregoing stock option will be subject to the Company's 2014 Equity Incentive Plan and standard form of stock option agreement (the "Option Agreement"), and shall provide that 25% of the shares vest after twelve (12) months, and the remaining 75% of the shares vest in equal monthly installments over the following thirty-six (36) months.

3. Confidentiality and Proprietary Information Obligations.

(a) Company Policies and Proprietary Information Agreement. You will be required to sign the Employee Proprietary Information and Inventions Assignment Agreement attached hereto as Exhibit A (the "Proprietary Information Agreement").

(b) Adverse or Outside Business Activities. Throughout your employment with the Company, you may engage in civic, academic teaching and lectures, and not-for profit activities so long as such activities do not interfere with the performance of your duties hereunder or present a conflict of interest with the Company. You may not engage in other employment or undertake any other commercial business activities unless you obtain the prior written consent of the Company's CEO. The Company may rescind its consent to your service as a director of all other corporations or participation in other business or public activities, if the Company, in its sole discretion, determines that such activities compromise or threaten to compromise the Company's reputational or business interests or conflict with your duties to the Company. In addition, throughout the term of your employment with the Company, you agree not to, directly or indirectly, without the prior written consent of the Company, own, manage, operate, join, control, finance or participate in the ownership, management, operation, control or financing of, or be connected as an officer, director, executive, partner, employee, principal, agent, representative, consultant, licensor, licensee or otherwise with, any business or enterprise engaged in any business which is competitive with or which is reasonably anticipated to be competitive with the Company's business; provided, however, that you may purchase or otherwise acquire up to (but not more than) one percent (1%) of any class of securities of any enterprise (but without participating in the activities of such enterprise) if such securities are listed on any national or regional securities exchange. You hereby represent and warrant that you have disclosed previously to the Board all other employment or other commercial business activities that you already undertake, or intend to undertake (to the extent currently known by you), during your period of employment with the Company.

4. No Conflicts.

By signing this Agreement you hereby represent to the Company that, except as previously disclosed to the Company: (a) your employment with the Company is not prohibited under any employment agreement or other contractual arrangement; and (b) you do not know of any conflicts which would restrict your employment with the Company. You hereby represent that you have disclosed to the Company any contract you have signed that may restrict your activities on behalf of the Company, and that you are presently in compliance with such contracts, if any.

5. At Will Employment.

Your employment relationship with the Company will be an "at-will" arrangement. The first ninety (90) days of employment at the Company are considered an Introductory Period. During this Introductory Period, the Company will evaluate your suitability for employment, and you can evaluate the Company. Neither your completion of the Introductory Period nor this Agreement constitute a guarantee of employment for any specific period of time. This means that either you or the Company may terminate your employment at any time, with or without cause, and with or without advance notice. This "at-will" employment relationship cannot be changed except in a written agreement approved by the Company and signed by you and by a duly authorized officer of the Company.

6. Miscellaneous.

As required by law, your employment is contingent upon satisfactory proof of your identity and legal authorization to work in the United States. Additionally, this offer is contingent upon verification of your references and satisfactory completion of a background check.

This Agreement, together with your Proprietary Information Agreement, forms the complete and exclusive statement of your employment agreement with the Company. The employment terms in this Agreement supersede any other agreements or promises made to you by anyone, whether oral or written, concerning your employment terms. The company will have the right to reassign you, to change your compensation, or to terminate your employment at any time, with or without cause or advance notice. This Agreement will bind the heirs, personal representatives, successors and assigns of both you and the Company, and inure to the benefit of both you and the Company, their heirs, successors and assigns. If any provision of this Agreement is determined to be invalid or unenforceable, in whole or in part, this determination shall not affect any other provision of this Agreement and the provision in question shall be modified so as to be rendered enforceable in a manner consistent with the intent of the parties insofar as possible under applicable law. This Agreement shall be construed and enforced in accordance with the laws of the State of California without regard to conflicts of law principles. Any ambiguity in this Agreement shall not be construed against either party as the drafter. Any waiver of a breach of this Agreement, or rights hereunder, shall be in writing and shall not be deemed to be a waiver of any successive breach or rights hereunder. This Agreement may be executed in counterparts which shall be deemed to be part of one original, and facsimile signatures shall be equivalent to original signatures.

Please sign and date this letter and return it to me by the close of business on May 6, 2015 in order to confirm your anticipated employment terms as set forth above.

We look forward to a productive and .enjoyable work relationship with you.

Sincerely,

Avalanche Biotechnologies, Inc.:

_____

Hans Hull, SVP Business Operations

Understood and Accepted:

_____

Jennifer Cheng

Date: _____

EXHIBIT A
EMPLOYEE PROPRIETARY INFORMATION AND INVENTIONS ASSIGNMENT AGREEMENT

A/7620813 1.I

Avalanche Biotechnologies, Inc.

EMPLOYEE CONFIDENTIALITY AND INVENTION ASSIGNMENT AGREEMENT

In partial consideration and as a condition of my employment by **AVALANCHE BIOTECHNOLOGIES,** (the **"Company"),** and effective as of the date that my employment by the Company first commenced as set forth below, I, the undersigned, agree as follows:

1. NONDISCLOSURE OF CONFIDENTIAL INFORMATION.

1.1. Confidential Information. During the term of my employment, I may receive and otherwise be exposed to confidential and proprietary information relating to the Company's business, strategies, designs and technologies, or to proprietary or confidential information relating to the Company's suppliers, customers or business partners. Such confidential and proprietary information may include but not be limited to confidential or proprietary information supplied to me with the legend "Confidential" or "Proprietary," or equivalent, and any of the following types of information, whether or not marked as confidential or proprietary: (i) information regarding physical or chemical or biological materials (such as, but not limited to, reagents, gene sequences, nucleic acids, cell lines, media, antibodies, compounds, c-DNAs, antisense nucleotides, proteins and vectors) and techniques for their handling and use; (ii) information regarding ideas, technology and processes (such as, but not limited to, assays, techniques, sketches, schematics, drawings, works of authorship, models, designs, inventions, know-how, technical documentation, equipment, algorithms, software programs, software source documents, formulae); (iii) information concerning or resulting from research and development projects and other projects (such as, but not limited to, preclinical and clinical data, design details and specifications, engineering information, and works in process); (iv) business and financial information (such as, but not limited to, current, future, and proposed products and services, financial information and models, information relating to procurement requirements, purchasing, manufacturing, customer lists, product plans, product ideas, business strategies, marketing or business plans, financial or personnel matters, investors, employees, business and contractual relationships, business forecasts, sales and merchandising, and information regarding third parties, suppliers, customers, employees, investors or facilities); (v) Inventions (as defined below), and (iv) information, derivatives, improvements or enhancements created using the foregoing information. (all of the above collectively referred to as **"Confidential Information").** I understand that Confidential Information shall not include information that (a) is in the public domain at the time of disclosure or enters the public domain following disclosure through no fault of mine, (b) is already in my possession prior to disclosure hereunder (as reflected by my written records), or (c) is required to be disclosed pursuant to an order of any competent court or government agency or rules of a securities exchange.

1.2. Duties. I acknowledge the confidential and secret character of the Confidential Information, and agree that the Confidential Information is the sole, exclusive and extremely valuable property of Company. Accordingly, I agree not to use the Confidential Information except in the performance of my authorized duties as an employee of Company, and not to disclose all or any part of the Confidential Information in any form to any third party, either during or after the term of my employment, without the prior written consent of the Company on a case-by-case basis. Appropriate prior written consent will be determined as follows: (i) if I am not an executive officer of the Company, then consent may be obtained from an executive officer of the Company, or (ii) if I am an executive officer of the Company, then from the Board of Directors of the Company. Upon termination of my employment, I agree to cease using and to return to Company all whole and partial copies and derivatives of the Confidential Information, whether in my possession or under my direct or indirect control, provided that I am entitled to retain my personal copies of (i) my compensation records, (ii) materials distributed to shareholders generally and (iii) this Agreement.

2. PROPERTY OF THE COMPANY. All notes, memoranda, reports, drawings, blueprints, manuals, materials, data, emails and other papers and records of every kind which shall come into my possession at any

time after the commencement of my employment with the Company, relating to any Inventions (as defined below) or Confidential Information, shall be the sole and exclusive property of the Company. This property shall be surrendered to the Company upon termination ofmy employment with the Company, or upon request by the Company, at any other time either during or after the termination of such employment. I further agree that in the event of termination of my employment with the Company I will execute a Termination Certificate substantially in the form attached hereto as Exhibit A.

3. INVENTIONS.

3.1. Disclosure. I shall disclose promptly in writing to an officer or to attorneys of the Company in accordance with the Company's policies and procedures any idea, invention, work of authorship, whether patentable or unpatentable, copyrightable or uncopyrightable, including, but not limited to, any documentation, formula, design, device, code, improvement, method, process, discovery, concept, development, machine or contribution, techniques, formulas, formulations, data, programs, organisms, plasmids, cosmids, bacteriophages, expression vectors, cells, cell lines, tissues, materials, substrates, media, delivery methods or transfection methods, assays, compounds, peptides, proteins, DNA, RNA, and their constructs, and sequence, genomic, and structural information relating thereto, crystals, optically active materials, ceramics, metals, metal oxides, and organic and inorganic chemical, biological and other material and their progeny, clones and derivatives and salt forms (any of the foregoing items hereinafter referred to as an **"Invention")** I may conceive, make, develop or work on, in whole or in part, solely or jointly with others, during the term of my employment with the Company. The disclosure required by this Section applies (a) during the period of my employment with the Company and for one year thereafter; (b) with respect to all Inventions whether or not they are conceived, made, developed or worked on by me during my regular hours of employment with the Company; (c) whether or not the Invention was made at the suggestion of the Company; (d) whether or not the Invention was reduced to drawings, written description, documentation, models or other tangible form; and (e) whether or not the Invention is related to the general line of business engaged in by the Company. The Company agrees that it will take reasonable precautions to keep Inventions disclosed to it pursuant to this Section 3.1 in confidence and shall not use any Inventions for its own advantage unless those Inventions are assigned or assignable to the Company pursuant to Section 3.2 or otherwise.

3.2. Assignment of Inventions to Company; Exemption of Certain Inventions. I hereby assign to the Company, and agree to assign automatically without requirement of further writing when first reduced to practice or recorded in a tangible medium, without royalty or any other further consideration, my entire right, title and interest in and to all Inventions and all intellectual property rights therein that (i) relate to the subject matters related to my employment and exist as of the date of this Agreement, for which I do not have an obligation to assign to any third party or (ii) I conceive, make, develop or work on during the period of my employment with the Company and for one year thereafter, except those Inventions that I develop entirely on my own time after the date of this Agreement without using the Company's equipment, supplies, facilities or Confidential Information, unless those Inventions either (a) relate at the time of conception or reduction to practice of the Invention to the Company's business, or actual or demonstrably anticipated research or development of the Company; or (b) result from or are related to any work performed by me for the Company, in which case I agree that any such Inventions shall also be automatically assigned to the Company. I acknowledge and agree that the Company has hereby notified me that the assignment provided for in Section 3.2(ii) does not apply to any Invention which qualifies fully for exemption from assignment under the provisions of Section 2870 of the California Labor Code, a copy of which is attached as Exhibit B. I also acknowledge and agree that nothing in this Section 3.2 above limits the assignment of any other rights in or to Confidential Information or other technology or intellectual property of the Company other than Inventions.

3.3. Records. I will make and maintain adequate and current written records of all Inventions covered by Section 3.1. These records shall be and remain the property of the Company.

3.4. Patents and Other Rights. Subject to Section 3.2, I will assist the Company in obtaining, maintaining and enforcing patents, invention assignments and copyright assignments, and other proprietary rights in connection with any Invention covered by Section 3.1, and otherwise will assist the Company as reasonably required by the Company to perfect in the Company the rights, title and other interests in my work product granted to the Company under this Agreement. Reasonable costs related to such assistance, if required, will be paid by the Company. I further agree that my obligations under this Section 3.4 shall continue beyond the termination of my employment with the Company, but if I am called upon to render such assistance after the termination of such employment, I shall be entitled to a fair and reasonable rate of compensation for such assistance. I shall, in addition, be entitled to reimbursement of any expenses incurred at the request of the Company relating to such assistance after the term of my employment. I hereby agree to waive any moral rights I may have in any copyrightable work I create on behalf of the Company. If the Company is unable for any reason, after reasonable effort, to secure my signature on any document needed in connection with the actions specified above, I hereby irrevocably designate and appoint the Company and its duly authorized officers and agents as. my agent and attorney in fact, which appointment is coupled with an interest, to act for and in my behalf to execute, verify and file any such documents and to do all other lawfully permitted acts to further the purposes of this Section 3.4 with the same legal force and effect as if executed by me.

3.5. Prior Contracts and Inventions; Information Belonging to Third Parties. I represent and warrant that, except as set forth on Exhibit C hereto, there are no other contracts to assign Inventions that are now in existence between any other person or entity and me. I further represent that (a) I am not obligated under any consulting, employment or other agreement which would affect the Company's rights or my duties under this Agreement, (b) there is no action, investigation, or proceeding pending or threatened, or any basis therefor known to me involving my prior employment or any consultancy or the use of any information or techniques alleged to be proprietary to any former employer, and (c) the performance of my duties as an employee of the Company will not breach, or constitute a default under any agreement to which I am bound, including, without limitation, any agreement limiting the use or disclosure of proprietary information acquired in confidence prior to engagement by the Company. I will not, in connection with my employment by the Company, use or disclose to the Company any confidential, trade secret or other proprietary information of any previous employer or other person to which I am not lawfully entitled. As a matter of record, I attach as Exhibit C of this Agreement a brief description of all Inventions made or conceived by me prior to my employment with the Company which I desire to be excluded from this Agreement **("Background Technology").** I hereby grant Company a non-exclusive, royalty-free, perpetual and irrevocable, worldwide right to use and sublicense the use of Background Technology for the purpose of developing, marketing, selling and supporting Company technology, products and services, either directly or through multiple tiers of distribution, but not for the purpose of marketing Background Technology separately from Company products or services.

4. NON-COMPETITION. During the term ofmy employment by the Company, I will not without the prior written approval of (i) an executive officer of the Company, in the event that I am not an executive officer of the Company, and (ii) the Board of Directors of the Company, in the event that I am an executive officer of the Company, (a) engage in any other professional employment or consulting, or (b) directly or indirectly participate in or assist any business which is a current or potential supplier, customer or competitor of the Company.

5. NON-SOLICITATION. During the term of my employment with the Company and for a period of one (1) year thereafter, I will not solicit or encourage, or cause others to solicit or encourage, any employees of the Company to terminate their employment with the Company. During the term of my employment with the Company, I will not solicit the business of any customer or client of the Company on my own behalf or on behalf of any person or entity other than the Company.

6. MISCELLANEOUS. The parties' rights and obligations under this Agreement will bind and inure to the benefit of their respective successors, heirs, executors, and administrators and permitted assigns. I will not assign this Agreement or its obligations hereunder without the prior written consent of the Company and any such purported assignment without consent shall be null and void from the beginning. This Agreement constitutes the parties' final, exclusive and complete understanding and agreement with respect to the subject matter hereof, and supersede all prior and contemporaneous understandings and agreements relating to its subject matter. This Agreement may not be waived, modified or amended unless mutually agreed upon in writing by both parties. In the event any provision of this Agreement is found to be legally unenforceable, such unenforceability shall not prevent enforcement of any other provision of the Agreement. I acknowledge that the Company will suffer substantial damages not readily ascertainable or compensable in terms of money in the event of the breach of any of my obligations under this Agreement. I therefore agree that the Company shall be entitled (without limitation of any other rights or remedies otherwise available to the Company) to obtain an injunction from any court of competent jurisdiction prohibiting the continuance or recurrence of any breach of this Agreement. The rights and obligations of the parties under this Agreement shall be governed in all respects by the laws of the State of California exclusively, without regard to conflict of law provisions. I agree that upon Company's request, all disputes arising hereunder shall be adjudicated in the state and federal courts having jurisdiction over disputes arising in San Francisco, California, and I hereby agree to consent to the personal jurisdiction of such courts. Any notices required or permitted hereunder shall be given to the appropriate party at the address specified above or at such other address as the party shall specify in writing. Such notice shall be deemed given upon personal delivery, or sent by certified or registered mail, postage prepaid, three (3) days after the date of mailing. This Agreement may be executed in any number of counterparts, each of which shall be deemed to be an original and all of which together shall be deemed to be one and the same instrument.

I **HAVE READ THIS AGREEMENT CAREFULLY AND** I **UNDERSTAND AND ACCEPT THE OBLIGATIONS WHICH IT IMPOSES UPON ME WITHOUT RESERVATION. NO PROMISES OR REPRESENTATIONS HAVE BEEN MADE TO ME TO INDUCE ME TO SIGN THIS AGREEMENT.** I **SIGN THIS AGREEMENT VOLUNTARILY AND FREELY,** IN **DUPLICATE, WITH THE UNDERSTANDING THAT THE COMPANY WILL RETAIN ONE COUNTERPART AND THE OTHER COUNTERPART WILL BE RETAINED BY ME.**

IN WITNESS WHEREOF, I have executed this document as of the ____ day of_____
20__

Employee

AGREED AND ACKNOWLEDGED:

Avalanche Biotechnologies

By: _____

Name: _____

Title: _____

EXHIBIT A

Termination Certificate

I, the undersigned, hereby certify that I do not have in my possession, nor have I failed to return, any documents or materials relating to the business of Company or its affiliates (the "Company"), or copies thereof, including, without limitation, any item of Confidential Information listed in Section 3 of the Company's Employee Confidentiality And Inventions Assignment Agreement (the "Agreement") to which I am a party.

I further certify that I have complied with all of the terms of the Agreement signed by me, including the reporting of any Inventions (as defined in the Agreement) covered by the Agreement.

I further agree that in compliance with the Agreement, I will preserve as confidential any information relating to the Company or any of it business partners, clients, consultants or licensees which has been disclosed to me in confidence during the course of my employment by the Company unless authorized in writing to do so (i) by an executive officer of the Company, in the event that I am not an executive officer of the Company, or (ii) by the Board of Directors of the Company, in the event that I am an executive officer of the Company.

Date: _____

(Employee's Signature)

_____

(Printed or Typed Name of Employee)

EXHIBIT B

California Labor Code

California Labor Code § 2870. Application of provision providing that employee shall assign or offer to assign rights in invention to **employer.**

(a) Any provision in an employment agreement which provides that an employee shall assign, or offer to assign, any of his or her rights in an invention to his or her employer shall not apply to an invention that the employee developed entirely on his or her own time without using the employer's equipment, supplies, facilities, or trade secret information except for those inventions that either:

(1) Relate at the time of conception or reduction to practice of the invention to the employer's business, or actual or demonstrably anticipated research or development of the employer; or

(2) Result from any work performed by the employee for the employer.

(b) To the extent a provision in an employment agreement purports to require an employee to assign an invention otherwise excluded from being required to be assigned under subdivision (a), the provision is against the public policy of this state and is unenforceable.

EXHIBIT C

BACKGROUND TECHNOLOGY

(List here prior contracts to assign Inventions that are now in existence between any other person or entity and you.)

none

(List here previous Inventions which you desire to have specifically excluded from the operation of this Agreement. Continue on reverse side if necessary.)

none

EXHIBIT B

AUTHORIZED OUTSIDE BUSINESS ACTIVITIES

Exhibit 10.36

ADVERUM BIOTECHNOLOGIES, INC.

CHANGE IN CONTROL AND SEVERANCE AGREEMENT

This Change in Control and Severance Agreement (the "Agreement") is made and entered into by and between _____ ("Executive") and Adverum Biotechnologies, Inc. (the "Company"), effective as of the latest date set forth by the signatures of the parties hereto below (the "Effective Date").

RECITALS

A. Executive and the Company are entering into an offer letter agreement, effective as of Executive's Hire Date as defined in therein (the "Offer Letter") concurrently with the execution of this Agreement.

B. It is expected that the Company from time to time will consider the possibility of an acquisition by another company or other change in control. The Board of Directors of the Company (the "Board") recognizes that such consideration as well as the possibility of an involuntary termination or reduction in responsibility can be a distraction to Executive and can cause Executive to consider alternative employment opportunities. The Board has determined that it is in the best interests of the Company and its stockholders to assure that the Company will have the continued dedication and objectivity of Executive, notwithstanding the possibility, threat or occurrence of such an event.

C. The Board believes that it is in the best interests of the Company and its stockholders to provide Executive with an incentive to continue Executive's employment and to motivate Executive to maximize the value of the Company upon a Change in Control (as defined below) for the benefit of its stockholders.

D. The Board believes that it is imperative to provide Executive with severance benefits upon certain terminations of Executive's service to the Company that enhance Executive's financial security and provide incentive and encouragement to Executive to remain with the Company notwithstanding the possibility of such an event.

E. Certain capitalized terms used in this Agreement are defined in Section 7 below.

The parties hereto agree as follows:

1. Term of Agreement. This Agreement shall become effective as of the Effective Date and terminate upon the date that all obligations of the parties hereto with respect to this Agreement have been satisfied.

2. At-Will Employment. The Company and Executive acknowledge that Executive's employment is and shall continue to be "at-will," as defined under applicable law. If

Executive's employment terminates for any reason, Executive shall not be entitled to any payments, benefits, damages, awards or compensation other than as provided by this Agreement.

3. Covered Termination Other Than During a Change in Control Period. If Executive experiences a Covered Termination other than during a Change in Control Period, and if Executive delivers to the Company a general release of all claims against the Company and its affiliates that becomes effective and irrevocable within sixty (60) days, or such shorter period of time specified by the Company, following such Covered Termination (a "Release of Claims"), then in addition to any accrued but unpaid salary, bonus, vacation and expense reimbursement payable in accordance with applicable law, the Company shall provide Executive with the following:

(a) Severance. Executive shall be entitled to receive an amount equal to nine (9) months of Executive's Base Salary, payable in substantially equal installments in accordance with the Company's normal payroll policies, less applicable withholdings; *provided, however,* that no payments under this Section 3(a) shall be made prior to the first payroll date occurring on or after the sixtieth (60th) day following the date of the Covered Termination (such payroll date, the "First Payroll Date"), and any amounts otherwise payable prior to the First Payroll Date shall be paid on the First Payroll Date without interest thereon.

(b) Continued Healthcare. If Executive elects to receive continued healthcare coverage pursuant to the provisions of the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended ("COBRA"), the Company shall directly pay, or reimburse Executive for, the premium for Executive and Executive's covered dependents through the earlier of (i) the nine (9)-month anniversary of the date of Executive's termination of employment and (ii) the date Executive and Executive's covered dependents, if any, become eligible for healthcare coverage under another employer's plan(s). Notwithstanding the foregoing, (i) if any plan pursuant to which such benefits are provided is not, or ceases prior to the expiration of the period of continuation coverage to be, exempt from the application of Section 409A of the Code under Treasury Regulation Section 1.409A-1(a)(5), or (ii) the Company is otherwise unable to continue to cover Executive under its group health plans without penalty under applicable law (including without limitation, Section 2716 of the Public Health Service Act), then, in either case, an amount equal to each remaining Company subsidy shall thereafter be paid to Executive in substantially equal monthly installments. After the Company ceases to pay premiums pursuant to this Section 3(b), Executive may, if eligible, elect to continue healthcare coverage at Executive's expense in accordance the provisions of COBRA.

4. Covered Termination During a Change in Control Period. If Executive experiences a Covered Termination during a Change in Control Period, and if Executive delivers to the Company a Release of Claims that becomes effective and irrevocable within sixty (60) days, or such shorter period of time specified by the Company, following such Covered Termination, then in addition to any accrued but unpaid salary, bonus, vacation and expense reimbursement payable in accordance with applicable law, the Company shall provide Executive with the following:

(a) Severance. Executive shall be entitled to receive an amount equal to the sum of: (i) twelve (12) months of the Executive's Base Salary at the rate in effect immediately

before the date of the Covered Termination and (ii) target annual bonus for the year in which Executive's termination occurs. Such amount shall be payable in a cash lump sum, less applicable withholdings, on the sixtieth (60th) day after the date of the Covered Termination.

(b) Equity Awards. Each outstanding equity award, including, without limitation, each stock option and restricted stock award, held by Executive shall automatically become vested and, if applicable, exercisable and any forfeiture restrictions or rights of repurchase thereon shall immediately lapse, in each case, with respect to one-hundred percent (100%) of the unvested shares of Company common stock subject to such equity award.

(c) Continued Healthcare. If Executive elects to receive continued healthcare coverage pursuant to the provisions of COBRA, the Company shall directly pay, or reimburse Executive for, the premium for Executive and Executive's covered dependents through the earlier of (i) the first anniversary of the date of Executive's termination of employment and (ii) the date Executive and Executive's covered dependents, if any, become eligible for healthcare coverage under another employer's plan(s). Notwithstanding the foregoing, (i) if any plan pursuant to which such benefits are provided is not, or ceases prior to the expiration of the period of continuation coverage to be, exempt from the application of Section 409A of the Code under Treasury Regulation Section 1.409A-1(a)(5), or (ii) the Company is otherwise unable to continue to cover Executive under its group health plans without penalty under applicable law (including without limitation, Section 2716 of the Public Health Service Act), then, in either case, an amount equal to each remaining Company subsidy shall thereafter be paid to Executive in substantially equal monthly installments. After the Company ceases to pay premiums pursuant to this Section 4(c), Executive may, if eligible, elect to continue healthcare coverage at Executive's expense in accordance the provisions of COBRA.

5. Other Terminations. If Executive's service with the Company is terminated by the Company or by Executive for any or no reason other than as a Covered Termination, then Executive shall not be entitled to any benefits hereunder other than accrued but unpaid salary, bonus, vacation and expense reimbursement in accordance with applicable law and to elect any continued healthcare coverage as may be required under COBRA or similar state law.

6. Limitation on Payments. Notwithstanding anything in this Agreement to the contrary, if any payment or distribution Executive would receive pursuant to this Agreement or otherwise ("Payment") would (a) constitute a "parachute payment" within the meaning of Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), and (b) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment shall either be (i) delivered in full, or (ii) delivered as to such lesser extent which would result in no portion of such Payment being subject to the Excise Tax, whichever of the foregoing amounts, taking into account the applicable federal, state and local income taxes and the Excise Tax; results in the receipt by Executive on an after-tax basis, of the largest payment, notwithstanding that all or some portion the Payment may be taxable under Section 4999 of the Code. The accounting firm engaged by the Company for general audit purposes as of the day prior to the effective date of the Change in Control shall perform the foregoing calculations. The Company shall bear all expenses with respect to the determinations by such accounting firm required to be made hereunder. The accounting firm shall provide its calculations to the Company and Executive within fifteen (15) calendar days after the date on

which Executive's right to a Payment is triggered (if requested at that time by the Company or Executive) or such other time as requested by the Company or Executive. Any good faith determinations of the accounting firm made hereunder shall be final, binding and conclusive upon the Company and Executive. Any reduction in payments and/or benefits pursuant to this Section 6 will occur in the following order: (1) reduction of cash payments; (2) cancellation of accelerated vesting of equity awards other than stock options; (3) cancellation of accelerated vesting of stock options; and (4) reduction of other benefits payable to Executive.

7. Definition of Terms. The following terms referred to in this Agreement shall have the following meanings:

(a) Base Salary. "Base Salary" means Executive's annual base salary in effect immediately prior to Executive's termination (disregarding any reduction in base salary that would give rise to Executive's right to a Constructive Termination).

(b) Cause. "Cause" will be determined in the sole discretion of the Board and will mean misconduct, including: (i) conviction of any felony or any crime involving moral turpitude or dishonesty; (ii) willful and material breach of Executive's duties that has not been cured within 30 days after written notice from the Board; (iii) intentional and material damage to the Company's property; or (iv) material breach of the Proprietary Information Agreement (as defined below).

(c) Change in Control. "Change in Control" shall mean the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) A transaction or series of transactions (other than an offering of Common Stock to the general public through a registration statement filed with the Securities and Exchange Commission) whereby any "person" or related "group" of "persons" (as such terms are used in Sections 13(d) and 14(d)(2) of the Securities Exchange Act of 1934, as amended (the "Exchange Act")) (other than the Company, any of its subsidiaries, an employee benefit plan maintained by the Company or any of its subsidiaries or a "person" that, prior to such transaction, directly or indirectly controls, is controlled by, or is under common control with, the Company) directly or indirectly acquires beneficial ownership (within the meaning of Rule 13d-3 under the Exchange Act) of securities of the Company possessing more than 50% of the total combined voting power of the Company's securities outstanding immediately after such acquisition; or

(ii) During any period of two consecutive years, individuals who, at the beginning of such period, constitute the Board together with any new director(s) (other than a director designated by a person who shall have entered into an agreement with the Company to effect a transaction described in Section 7(c)(i) or 7(c)(ii)) whose election by the Board or nomination for election by the Company's stockholders was approved by a vote of at least two-thirds of the directors then still in office/who either were directors at the beginning of the two-year period or whose election or nomination for election was previously so approved, cease for any reason to constitute a majority thereof; or

(iii) The consummation by the Company (whether directly involving the Company or indirectly involving the Company through one or more intermediaries) of (x) a merger, consolidation, reorganization, or business combination or (y) a sale or other disposition of all or substantially all of the Company's assets in any single transaction or series of related transactions or (z) the acquisition of assets or stock of another entity, in each case other than a transaction: (A) which results in the Company's voting securities outstanding immediately before the transaction continuing to represent (either by remaining outstanding or by being converted into voting securities of the Company or the person that, as a result of the transaction, controls, directly or indirectly, the Company or owns, directly or indirectly, all or substantially all of the Company's assets or otherwise succeeds to the business of the Company (the Company or such person, the "Successor Entity")) directly or indirectly, at least a majority of the combined voting power of the Successor Entity's outstanding voting securities immediately after the transaction, and (B) after which no person or group beneficially owns voting securities representing 50% or more of the combined voting power of the Successor Entity; provided, however, that no person or group shall be treated for purposes of this clause (B) as beneficially owning 50% or more of the combined voting power of the Successor Entity solely as a result of the voting power held in the Company prior to the consummation of the transaction; or

(iv) The Company's stockholders approve a liquidation or dissolution of the Company.

Notwithstanding the foregoing, in no event shall a transaction constitute a Change in Control unless such transaction also constitutes a "change in control event" within the meaning of Section 409A of the Code and the Treasury regulations promulgated thereunder.

(d) Change in Control Period. "Change in Control Period" means the period of time beginning three (3) months prior to and ending twelve (12) months following a Change in Control.

(e) Constructive Termination. "Constructive Termination" means any of the following actions taken without Cause by the Company or a successor corporation or entity without Executive's consent: (i) substantial reduction of Executive's rate of compensation; (ii) material reduction in Executive's duties, provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" unless Executive's new duties are substantially reduced from the prior duties, and changes in Executive's duties and responsibilities in connection with changes in the Company's businesses and prospects and/or changes to Executive's reporting relationship such that Executive reports to an executive officer of the Company other than the Chief Executive Officer shall not be deemed a "material reduction" in Executive's duties; (iii) failure or refusal of a successor to the Company to assume the Company's obligations under this Agreement in the event of a Change in Control; (iv) relocation of Executive's principal place of employment or service to a place greater than 50 miles from the Executive's then current principal place of employment or service; (v) the requirement to increase the amount of time per week that Executive provides services to the Company or (vi) the requirement that the Executive cease other employment or consulting engagements, unless such employment and/or consulting engagement results in a conflict with the Company's business. Notwithstanding the foregoing, a resignation shall not constitute a "Constructive Termination" unless the event or condition giving rise to such resignation

continues more than thirty (30) days following Executive's written notice of such condition provided to the Company within ninety (90) days of the first occurrence of such event or condition and such resignation is effective within thirty (30) days following the end of such notice period.

(f) Covered Termination. "Covered Termination" shall mean Executive's Constructive Termination or the termination of Executive's employment by the Company other than for Cause.

8. Successors.

(a) Company's Successors. Any successor to the Company (whether direct or indirect and whether by purchase, merger, consolidation, liquidation or otherwise) to all or substantially all of the Company's business and/or assets shall assume the obligations under this Agreement and agree expressly to perform the obligations under this Agreement in the same manner and to the same extent as the Company would be required to perform such obligations in the absence of a succession. For all purposes under this Agreement, the term "Company" shall include any successor to the Company's business and/or assets which executes and delivers the assumption agreement described in this Section 8(a) or which becomes bound by the terms of this Agreement by operation of law.

(b) Executive's Successors. The terms of this Agreement and all rights of Executive hereunder shall inure to the benefit of, and be enforceable by, Executive's personal or legal representatives, executors, administrators, successors, heirs, distributees, devisees and legatees.

9. Notices. Notices and all other communications contemplated by this Agreement shall be in writing and shall be deemed to have been duly given when personally delivered or one day following mailing via Federal Express or similar overnight courier service. In the case of Executive, mailed notices shall be addressed to Executive at Executive's home address that the Company has on file for Executive. In the case of the Company, mailed notices shall be addressed to its corporate headquarters, and all notices shall be directed to the attention of its Legal Department.

10. Confidentiality; Non-Solicitation.

(a) Confidentiality. Nothing herein modifies, supersedes, voids or otherwise alters Executive's pre-existing contractual obligations set forth in the Employee Proprietary Information and Invention Assignment Agreement ("Proprietary Information Agreement") entered into between Executive and the Company.

(b) Non-Solicitation. In addition to Executive's obligations under the Proprietary Information Agreement, Executive shall not for a period of one (1) year following Executive's termination of employment for any reason, either on Executive's own account or jointly with or as a manager, agent, officer, employee, consultant, partner, joint venturer, owner or stockholder or otherwise on behalf of any other person, firm or corporation, directly or indirectly solicit or attempt to solicit away from the Company any of its officers or employees or offer employment to any person who is an officer or employee of the Company; *provided,*

however, that a general advertisement to which an employee of the Company responds shall in no event be deemed to result in a breach of this Section 10(b). Executive also agrees not to harass or disparage the Company or its employees, clients, directors or agents or divert or attempt to divert any actual or potential business of the Company.

(c) Survival of Provisions. The provisions of this Section 10 shall survive the termination or expiration of the applicable Executive's employment with the Company and shall be fully enforceable thereafter. If it is determined by a court of competent jurisdiction in any state that any restriction in this Section 10 is excessive in duration or scope or is unreasonable or unenforceable under the laws of that state, it is the intention of the parties that such restriction may be modified or amended by the court to render it enforceable to the maximum extent permitted by the law of that state.

11. Dispute Resolution. To ensure the timely and economical resolution of disputes that arise in connection with this Agreement, Executive and the Company agree that any and all disputes, claims, or causes of action arising from or relating to the enforcement, breach, performance or interpretation of this Agreement, Executive's employment, or the termination of Executive's employment, shall be resolved to the fullest extent permitted by law by final, binding and confidential arbitration, by a single arbitrator, in San Mateo County, California, conducted by Judicial Arbitration and Mediation Services, Inc. ("JAMS") under the applicable JAMS employment rules. **By agreeing to this arbitration procedure, both Executive and the Company waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding.** The arbitrator shall: (i) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be permitted by law; and (ii) issue a written arbitration decision, to include the arbitrator's essential findings and conclusions and a statement of the award. The arbitrator shall be authorized to award any or all remedies that Executive or the Company would be entitled to seek in a court of law. The Company shall pay all JAMS' arbitration fees in excess of the amount of court fees that would be required if the dispute were decided in a court of law. Nothing in this Agreement is intended to prevent either Executive or the Company from obtaining injunctive relief in court pursuant to Section 1281.8 of the California Code of Civil Procedure to prevent irreparable harm pending the conclusion of any such arbitration. Notwithstanding the foregoing, Executive and the Company each have the right to resolve any issue or dispute over intellectual property rights by Court action instead of arbitration.

12. Miscellaneous Provisions.

(a) Section 409A.

(i) Separation from Service. Notwithstanding any provision to the contrary in this Agreement, no amount deemed deferred compensation subject to Section 409A of the Code shall be payable pursuant to Sections 3 or 4 unless Executive's termination of employment constitutes a "separation from service" with the Company within the meaning of Section 409A of the Code and the Department of Treasury regulations and other guidance promulgated thereunder ("Separation from Service") and, except as provided under Section 12(a)(ii) of this Agreement, any such amount shall not be paid, or in the case of installments, commence payment, until the sixtieth (60th) day following Executive's Separation from Service.

Any installment payments that would have been made to Executive during the sixty (60) day period immediately following Executive's Separation from Service but for the preceding sentence shall be paid to Executive on the sixtieth (60th) day following Executive's Separation from Service and the remaining payments shall be made as provided in this Agreement.

(ii) Specified Employee. Notwithstanding any provision to the contrary in this Agreement, if Executive is deemed at the time of his or her separation from service to be a "specified employee" for purposes of Section 409A(a)(2)(B)(i) of the Code, to the extent delayed commencement of any portion of the benefits to which Executive is entitled under this Agreement is required in order to avoid a prohibited distribution under Section 409A(a)(2)(B)(i) of the Code, such portion of Executive's benefits shall not be provided to Executive prior to the earlier of (a) the expiration of the six (6)-month period measured from the date of the Executive's Separation from Service or (b) the date of Executive's death. Upon the first business day following the expiration of the applicable Code Section 409A(a)(2)(B)(i) period, all payments deferred pursuant to this Section 12(a)(ii) shall be paid in a lump sum to Executive, and any remaining payments due under this Agreement shall be paid as otherwise provided herein.

(iii) Expense Reimbursements. To the extent that any reimbursements payable pursuant to this Agreement are subject to the provisions of Section 409A of the Code, any such reimbursements payable to Executive pursuant to this Agreement shall be paid to Executive no later than December 31 of the year following the year in which the expense was incurred, the amount of expenses reimbursed in one year shall not affect the amount eligible for reimbursement in any subsequent year, and Executive's right to reimbursement under this Agreement will not be subject to liquidation or exchange for another benefit.

(b) Waiver. No provision of this Agreement shall be modified, waived or discharged unless the modification, waiver or discharge is agreed to in writing and signed by Executive and by an authorized officer of the Company (other than Executive). No waiver by either party of any breach of, or of compliance with, any condition or provision of this Agreement by the other party shall be considered a waiver of any other condition or provision or of the same condition or provision at another time.

(c) Whole Agreement. This Agreement, the Offer Letter, and Executive's Proprietary Information Agreement represent the entire understanding of the parties hereto with respect to the subject matter hereof and supersede all prior arrangements and understandings regarding same, including, without limitation, any accelerated vesting provisions of any stock option agreement between the Company and Executive.

(d) Choice of Law. The validity, interpretation, construction and performance of this Agreement shall be governed by the laws of the State of California.

(e) Severability. The invalidity or unenforceability of any provision or provisions of this Agreement shall not affect the validity or enforceability of any other provision hereof, which shall remain in full force and effect.

(f) Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together will constitute one and the same instrument.

IN WITNESS WHEREOF, each of the parties has executed this Agreement, in the case of the Company by its duly authorized officer, as of the day and year set forth below.

ADVERUM BIOTECHNOLOGIES, INC.

By: _____

Title:

Date:

EXECUTIVE

By: _____

Date: _____

Exhibit 10.43

RELEASE AGREEMENT

This Release Agreement (this "**Agreement**") is entered into as of October 3, 2017 between Steven Schwartz, M.D. ("**Director**") and Adverum Biotechnologies, Inc. (the "**Company**").

Whereas, Director has served as a member of the Company's Board of Directors (the "**Board**") since September 2010 and has advised the Company of his decision to resign from the Board effective October 3, 2017; and

Whereas, in recognition of Director's long service as a director, the Executive Committee of the Board has approved and separately communicated with Director regarding an extension of the post-termination exercise period applicable to Director's stock options under the Company's 2014 Equity Incentive Award Plan, which separate communication is attached hereto; and

Whereas, in consideration of such extension and for other valuable consideration, Director is entering into this Release Agreement;

Now, **Therefore**, the parties hereby agree as follows:

1. Release of Claims. Director hereby releases the Company and its affiliated, related, parent and subsidiary entities, and their current and former directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, insurers, affiliates, and assigns (collectively, the "**Released Parties**") from any and all claims, liabilities, or obligations of every kind and nature, whether known or unknown, arising at any time prior to or at the time this Agreement is signed (collectively, the "**Released Claims**"). The Released Claims include, but are not limited to: all federal, state and local constitutional, statutory and common law claims; claims directly or indirectly arising out of or in any way connected with the relationship between Director and the Company or the termination of that relationship; and claims for breach of contract or other promise, fraud, misrepresentation, discrimination, harassment, retaliation, emotional distress, compensation, commissions, benefits, or equity interests. In giving this release, Director acknowledges having read and understood Section 1542 of the California Civil Code, which provides: "**A general release does not extend to claims which the creditor does not know or suspect to exist in his or her favor at the time of executing the release, which if known by him or her must have materially affected his or her settlement with the debtor**." Director expressly waives and relinquishes all rights and benefits under that section and any law of any jurisdiction of similar effect with respect to Director's release of claims herein, including but not limited to the release of unknown claims.

2. Excluded Claims. Notwithstanding the foregoing, the following are not included in the Released Claims (the "**Excluded Claims**"): (1) all rights or claims for indemnification, a defense and/or to be held harmless, in all cases to the fullest extent provided for, that Director may have pursuant to any written indemnification agreement with the Company to which Director is a party, the charter, Certificate of Incorporation or bylaws of the Company, under applicable law, or otherwise; (2) all rights which are not waivable as a matter of law; (3) all rights arising out of this Agreement; (4) all rights under any insurance policy; and (5) all rights in and to Director's

Company equity, including, without limitation, Director's right to exercise, hold and sell Company equity. Director hereby represents and warrants that, other than the Excluded Claims, Director is not aware of any claims Director has or might have against any of the Released Parties that are not included in the Released Claims. The Company hereby represents and warrants that it is not aware of any claims the Company has or might have against Director.

3. General. This Agreement constitutes the complete and exclusive embodiment of the entire agreement between the Company and Director with regard to the subject matter hereof. Director is not relying on any promise or representation, written or oral, that is not expressly stated herein. This Agreement may only be modified or amended by a written agreement signed by both Director and a duly authorized representative of the Company. If any provision of this Agreement is determined to be unenforceable, in whole or in part, such determination will not affect any other provision of this Agreement and the provision in question shall be deemed modified so as to be rendered enforceable in a manner consistent with the intent of the parties insofar as possible under applicable law. This Agreement shall be governed by the laws of the State of California without regard to conflicts of law principles. Any ambiguity in this Agreement shall not be construed against either party as the drafter. Any waiver of a breach of this Agreement, or rights hereunder, shall be in writing and shall not be deemed a waiver of any successive breach or rights hereunder. Director shall have no duty to mitigate any breach by the Company of this Agreement.

The parties have executed this Agreement as of the date first written above.

/s/ Steven Scwartz
Steven Schwartz, M.D.

ADVERUM BIOTECHNOLOGIES, INC.

By: /s/ Amber Salzman
Amber Salzman
President and Chief Executive Officer

Exhibit 21.1

SUBSIDIARIES OF ADVERUM BIOTECHNOLOGIES, INC.

Name of Subsidiary	Country of Incorporation
Avalanche Australia PTY LTD	Australia
Adverum Biotechnologies, SAS	France
Annapurna Therapeutics, LTD	Ireland

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statements No. 333-219890 on Form S-3 and S-3/A and No. 333-220894, No. 333-218465, No. 333-211439, No. 333-203398, and No. 333-199296 on Form S-8 of our report dated March 6, 2017, relating to the consolidated financial statements of Adverum Biotechnologies, Inc. and its subsidiaries appearing in this Annual Report on Form 10-K of Adverum Biotechnologies, Inc. for the year ended December 31, 2017.

/s/ Deloitte & Touche LLP

San Jose, California
March 6, 2018

Exhibit 31.1

CERTIFICATION OF THE PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Amber Salzman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Adverum Biotechnologies, Inc.;

2. Based on my knowledge, this annual 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 annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual 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 annual 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 we 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 annual report based on such evaluation; and

   d. Disclosed in this annual 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; and

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 6, 2018

By: /s/ Amber Salzman
Name: Amber Salzman
Title: President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION
PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Leone Patterson, certify that:

1. I have reviewed this Form 10-K of Adverum Biotechnologies, 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; and

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 6, 2018

By: /s/ Leone Patterson
Name: Leone Patterson
Title: Chief Financial Officer
(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 on Form 10-K of Adverum Biotechnologies, Inc. for the year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Amber Salzman, as President and Chief Executive Officer of Adverum Biotechnologies, Inc., hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of her knowledge, the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of Adverum Biotechnologies, Inc.

Date: March 6, 2018

By: /s/ Amber Salzman
Amber Salzman
President and Chief Executive Officer
(Principal Executive Officer)

In connection with the Annual Report on Form 10-K of Adverum Biotechnologies, Inc. for the year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Leone Patterson, as Chief Financial Officer of Adverum Biotechnologies, Inc., hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to the best of her knowledge, the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of Adverum Biotechnologies, Inc.

Date: March 6, 2018

By: /s/ Leone Patterson
Leone Patterson
Chief Financial Officer
(Principal Financial and Accounting Officer)