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, 2018

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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files): Yes ☒ No ☐

Indicate by check mark 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.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐	Smaller reporting company	☒
		Emerging growth company	☒

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

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

As of June 30, 2018, 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 $294.8 million, based on the closing price of the registrant's common stock on the Nasdaq Global Market on June 30, 2018 of $5.30 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, 2019, the registrant had 63,201,009 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 2019 Annual Meeting of Stockholders of the registrant are incorporated by reference into Part III of this Annual Report on Form 10-K. If the Proxy Statement is not filed by April 30, 2019, then the registrant will file an amendment to this Form 10-K on Form 10-K/A to include the Part III information in this Form 10-K.

TABLE OF CONTENTS

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.

Adverum, the Adverum logo and other trademarks or service marks of Adverum that may appear in this Annual Report on Form 10-K are the property of Adverum. This Annual Report on Form 10-K contains additional trade names, trademarks, and service marks of other companies.

Adverum does not intend its use or display of other companies' trade names, trademarks, or service marks to imply a relationship with, or endorsement or sponsorship of Adverum by, these other companies, and all such third-party trade names, trademarks, and service marks are the property of their respective owners.

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 ocular 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 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.

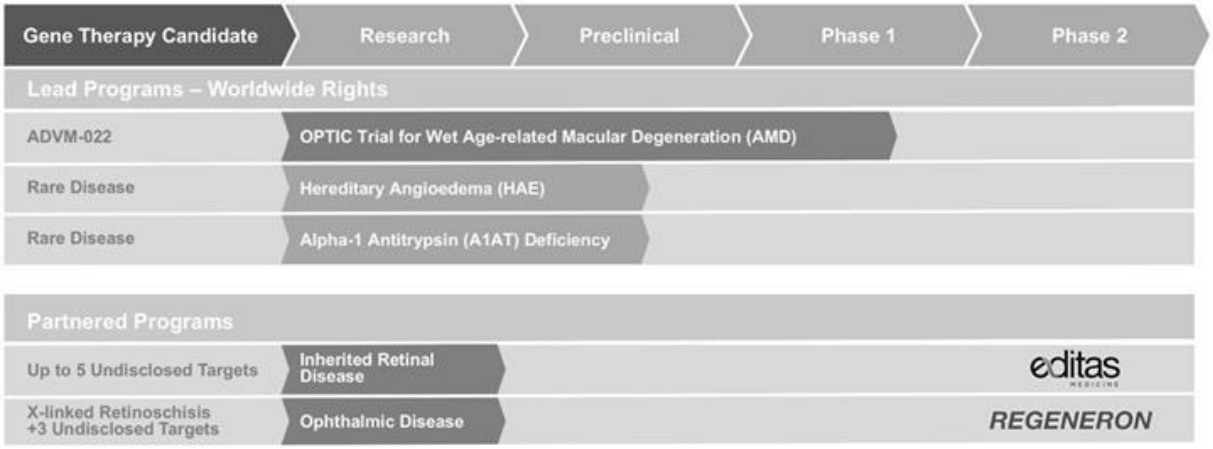
PART 1.

Item 1. Business

Overview

Adverum is a clinical-stage gene therapy company targeting unmet medical need in ocular and rare diseases. We develop gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. Our core capabilities include clinical development, novel vector discovery, and in-house manufacturing expertise, specifically in scalable process development, assay development, and current Good Manufacturing Practices ("cGMP") quality control.

We are advancing a pipeline of novel gene therapy product candidates designed to treat ocular and rare diseases. Our pipeline of internal programs and partnered programs is shown below.



We are conducting a clinical trial for our most advanced gene therapy candidate ADVM-022, AAV.7m8-aflibercept, for the treatment of wet age-related macular degeneration (wet AMD). ADVM-022 uses a proprietary capsid ("AAV.7m8") to deliver a proprietary expression cassette which expresses aflibercept. ADVM-022 is administered as a single intravitreal injection and is designed to minimize the treatment burden of repeated anti-Vascular Endothelial Growth Factor ("VEGF") injections, which is the current standard of care for the treatment of wet AMD. In November 2018, we dosed the first patient in the ADVM-022 Phase 1 clinical trial entitled "An Open Label Phase 1 Study of ADVM-022 (AAV.7m8-aflibercept) in Neovascular (Wet) Age-Related Macular Degeneration ("OPTIC trial"). We expect to provide an update on enrollment from the OPTIC trial in the first half of 2019. In addition, we expect to provide interim data from the OPTIC trial by the first quarter of 2020.

We collaborate with other industry leaders in order to leverage our expertise to develop gene therapy candidates. We have entered into collaboration agreements with Editas Medicine, Inc. ("Editas") and Regeneron Pharmaceuticals, Inc. ("Regeneron"). In addition, we have licensed the right to use AAV.7m8 to GenSight Biologics S.A. ("GenSight").

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 development capabilities in adeno- associated virus ("AAV") technology;
- a pipeline of gene therapy product candidates targeting the treatment of ocular and rare diseases;
- in-house manufacturing expertise, specifically in scalable process development, assay development, and cGMP quality control;
- a growing portfolio of proprietary vectors;
- a robust patent portfolio; 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 ocular and rare diseases. The key elements of our strategy to achieve this goal are to:

- **Target large patient population impacted by wet AMD.** There are an estimated 1.2 million individuals in the U.S. and 3 million worldwide living with wet AMD, and the incidence of new cases is expected to continue to grow significantly as the population ages. We estimate that the standard-of-care therapies generated in excess of $10 billion worldwide in sales in 2018.
- **Address unmet medical need by supplanting chronic treatment regimens with a one-time gene therapy treatment.** Our gene therapies are designed as single-administration treatments to address the unmet needs of patients with ocular and rare diseases. The current standard of care for wet AMD and many rare diseases require frequent injections for the duration of the disease, which represent significant treatment burden for patients and their care-takers. As an example, for wet AMD, the current standard-of-care treatments require patients to receive intravitreal injections of anti-VEGF protein every 4-12 weeks, which can be difficult for patients to comply with, leading to loss of vision from underdosing. A single-dose gene therapy has the potential to alleviate this treatment burden.
- **Pursue indications with well-defined clinical and regulatory paths where possible, 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, for wet AMD, aflibercept is an approved standard-of-care treatment, and ADVM-022 utilizes a proprietary vector designed to provide the same anti-VEGF protein through a single intravitreal injection. We are evaluating whether other ocular diseases with approved anti-VEGF therapies might also be treated with ADVM-022.
- **Advance our earlier-stage research initiatives and leverage our industry-leading capabilities in novel vector development.** We leverage our next-generation AAV-based directed evolution platform to engineer AAV capsids with enhanced tropism for certain tissues and/or improved antibody neutralization profiles over existing AAV variants. Combining our vectorology and manufacturing expertise, we have the capability to generate high-quantity recombinant AAV capsid libraries that can be screened in large animals rather than rodents, to maximize applicability of the screens to human subjects. We are also focused on discovering improved ubiquitous and cell-specific promoters and expression cassettes to offer optimal transgene expression target tissues. We plan to use this expertise to expand our pipeline and manage the life cycle of our novel gene therapies.
- **Collaborate with partners to leverage our industry-leading AAV vector expertise and ocular 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 that may benefit from our capabilities and expertise in AAV vector development and product delivery.
- **Expand our process development capabilities to support late-stage clinical trials and commercialization.** We are investing in a facility which will allow us to expand our internal process development capabilities. Our manufacturing process is based on the Baculovirus/Sf9 production system, which has been used for a number of vaccines and recombinant protein therapies approved by the U.S. Food and Drug Administration ("FDA") and European Medical Agency ("EMA"), and is capable of producing large quantities of AAVs. Our strategy is to develop scalable processes to transfer to our cGMP contract manufacturers, commensurate with our stage of development. Our new facility will expand our in-house process development capabilities to support larger, late-stage clinical trials and commercialization.

Gene Therapy Background

Gene therapy is a powerful treatment modality to address disease biology in a targeted and efficient way. With gene therapy, patients receive vectors encoding therapeutic genes, expressing a therapeutic protein or the functional version of a mutated protein. 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 potentially are 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:

- **Substantial clinical data.** Positive data from gene therapy clinical trials have been reported in a variety of indications, including hemophilia, Spinal Muscular Atrophy, X-linked myotubular myopathy, Sanfilippo syndrome, ornithine transcarbamylase deficiency, glycogen storage disease type 1a, and Duchenne muscular dystrophy, as well as several ocular diseases including biallelic RPE65 mutation-associated retinal dystrophy, choroideremia, and X-linked retinitis pigmentosa.
- **Significant investment by biopharmaceutical companies.** The modality of gene therapy has received significant interest and investments by biopharmaceutical companies. Large, global biopharmaceutical companies, such as BioMarin Pharmaceutical Inc., Biogen Idec Inc., Celgene Corporation, GlaxoSmithKline plc, Hoffmann-La Roche Ltd., Novartis, Regeneron, Sanofi, 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., REGENXBIO Inc., Spark Therapeutics, Inc., Ultragenyx Pharmaceutical Inc., uniQure N.V., Abeona Therapeutics, Nightstar Therapeutics, Sarepta Therapeutics, Solid Biosciences, and Voyager Therapeutics, have attracted recent investment in this growing field.
- **Approval of cell and gene therapy products by regulatory authorities.** The FDA and EMA have approved several cell and gene therapy products. In December 2017, the FDA 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, which carry a therapeutic DNA instead of the viral genes. The resulting vector is used to deliver a gene into a desired cell population, which when expressed, can provide sustained 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.** Naturally occurring AAV is not known to cause disease in humans.
- **Non-replicating.** Naturally occurring AAV is incapable of replication without co-infection of a helper virus such as adenovirus, herpes virus, or others. Once inside the host cell, AAV vectors do not replicate, and cannot spread in the absence of co-infection.
- **Long-term expression.** Once incorporated into the host cell, AAV vectors can continue to drive expression of a therapeutic protein for years, making AAV-based gene therapy a compelling treatment modality for diseases requiring frequent chronic treatment regimens.
- **Low-integrating potential.** AAV vector genomes remain mainly as a stable non-integrated episome in the host cell nucleus, mitigating safety concerns associated with genomic integration.
- **Low inflammatory potential.** Compared to other vectors used in direct gene therapy approaches, AAV vectors elicit mild inflammatory reactions.
- **Ability to transduce non-dividing cells.** AAV vectors can 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 (wet AMD) or its natural organ of production (A1AT).
- **FDA approved.** In December 2017, the FDA 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.

AAV-derived vectors are a leading vector used in gene therapy. According to the *Journal of Gene Medicine*, AAV has been used in over 200 clinical trials as of August 2018. As effective as existing AAV vectors are in gene therapy, we believe there are opportunities for improvement. Naturally occurring AAV variants have evolved with particular characteristics, some of which remain and pose limitations to their use in gene therapy.

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, we screen the AAVs in the pool for novel properties, e.g., specific transduction of a particular cell type, or the capability to evade pre-existing neutralizing immune response. Once capsids with desirable properties are identified, those capsids are screened to create a smaller pool of optimized vectors which are further screened until we have identified a select number of engineered AAVs with the characteristics we seek.

Our Product Candidates

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

Ocular Diseases

ADVM-022 for Treatment of Wet AMD

Market for Treating Patients with Wet AMD

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.

Wet AMD is an advanced form of AMD, affecting approximately 10% of patients living with AMD. In patients with wet AMD, blood vessels begin to invade the 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.

Wet AMD is a leading cause of vision loss in patients over 60 years of age, with a prevalence of approximately 1.2 million individuals in the U.S. and 3 million worldwide. The incidence of new cases of wet AMD in the U.S. is approximately 150,000 to 200,000 annually, and this number is expected to grow significantly as the country's population ages.

Although the underlying molecular causes of wet AMD are not completely known, VEGF is known to play a central role in the growth of new blood vessels in wet AMD. The current standard-of-care therapies for wet AMD are proteins that bind VEGF and neutralize its activity. We estimate that these standard-of-care therapies generated in excess of $10 billion in sales worldwide in 2018.

The standard-of-care therapies for wet AMD can be burdensome, as patients generally require chronic intravitreal injection of anti-VEGF protein every 4-12 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 Treating Wet AMD

ADVM-022 is our clinical-stage gene therapy product candidate for the treatment of wet AMD. ADVM-022 uses the AAV.7m8 capsid to deliver a proprietary expression cassette expressing aflibercept. ADVM-022 is administered as a single intravitreal injection and is designed to minimize the treatment burden of frequent injections required for the standard-of-care treatment. The AAV.7m8 capsid was engineered from AAV2 by directed evolution to efficiently transduce retinal cells following intravitreal injection. The vector carries a vector genome ("vg") encoding a codon-optimized cDNA of the aflibercept protein, a current standard of care in wet AMD, under the control of a strong, ubiquitous expression cassette.

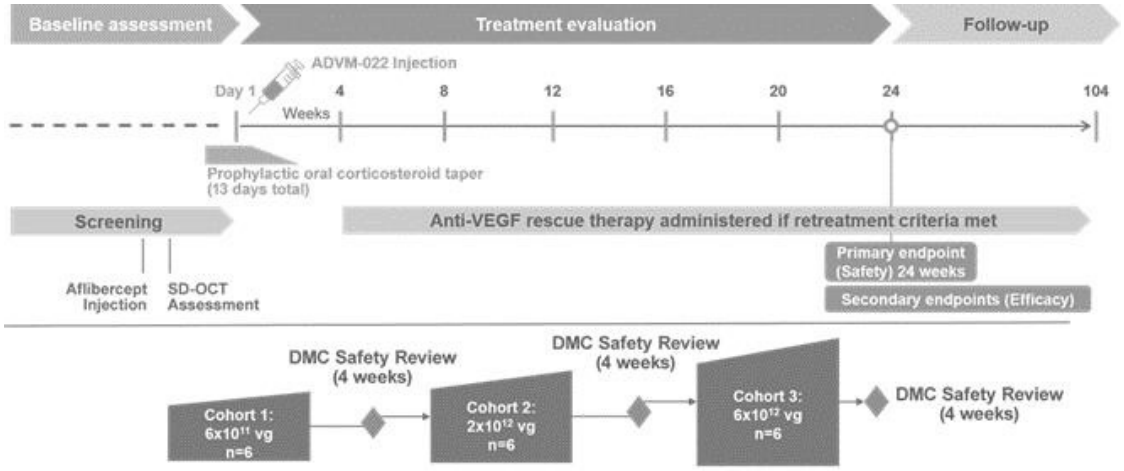
A number of AAV-based gene therapy products, including LUXTURNA, are designed for subretinal injection. However, we believe intravitreal injection of gene therapy offers substantial benefits over subretinal injection, including:

- intravitreal injection is the current standard of care for wet AMD patients, and more widely used than subretinal injections;
- vector delivered by subretinal injection can only access cells near the injection site (the "bleb"), whereas intravitreal injection allows the vector to access a larger portion of the retinal surface area; and
- subretinal injections require a surgical setting, while intravitreal injections are administered in an outpatient visit.

Advancing the Clinical Development of ADVM-022 for Wet AMD

We initiated the ADVM-022 Phase 1 clinical trial entitled "An Open Label Phase 1 Study of ADVM 022 (AAV.7m8-aflibercept) in Neovascular (Wet) Age-Related Macular Degeneration – [OPTIC]" ("the OPTIC trial") with the first patient dosed in November 2018.

The OPTIC trial is a multi-center, open-label, Phase 1, dose-escalation trial, designed to assess the safety and tolerability of a single intravitreal injection of ADVM-022 in patients with wet AMD who are responsive to anti-VEGF treatment. The trial is expected to enroll 18 patients and evaluate three doses of ADVM-022; first dose: 6×10^{11} vg/eye, second dose: 2×10^{12} vg/eye, and third dose: 6×10^{12} vg/eye. Subjects will be administered a tapering prophylactic corticosteroid regimen. The primary endpoint of the trial is the safety and tolerability of ADVM-022 at 24 weeks after a single intravitreal injection. Secondary endpoints include changes in best-corrected visual acuity ("BCVA"), measurement of central retinal thickness ("CRT"), as well as mean number of rescue anti-VEGF injections and percentage of patients needing rescue anti-VEGF injections. The OPTIC trial will last approximately two years. A diagram of the OPTIC trial is shown below.



We expect to provide an update on enrollment from the OPTIC trial in the first half of 2019. In addition, we expect to provide interim data from the OPTIC trial by the first quarter of 2020.

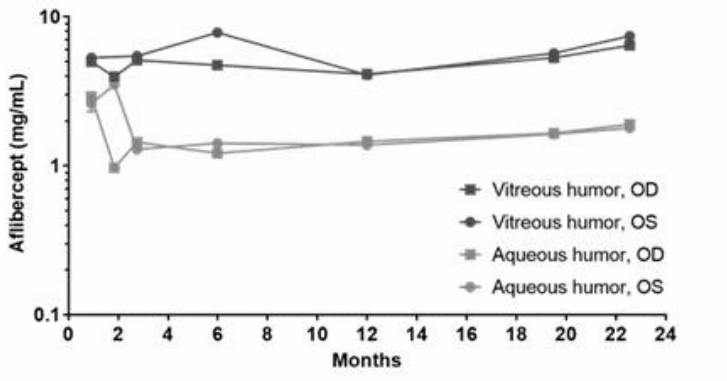
In September 2018, we received Fast Track designation from the FDA for ADVM-022 for wet AMD. The Fast Track designation is given to drugs and biologics that treat serious conditions and fill unmet medical need. Fast Track designation makes ADVM-022 for wet AMD eligible for several benefits, including more frequent meetings with the FDA to discuss our development plan, more frequent written communications, and rolling review our Biological License Application ("BLA").

Beyond wet AMD, we are evaluating whether other ocular diseases with approved anti-VEGF therapies might also be treated with ADVM-022.

Preclinical Proof of Concept for ADVM-022

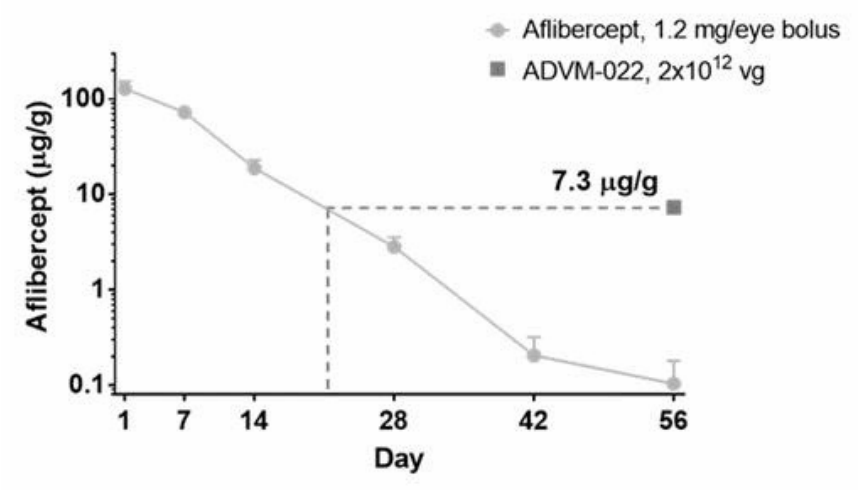
ADVM-022 was designed to provide long-term aflibercept expression following intravitreal injection. To evaluate the potential of ADVM-022 to treat wet AMD, we assessed its efficacy non-human primates ("NHPs"). We observed that a single intravitreal administration of ADVM-022 provided sustained expression of aflibercept for at least two years at levels comparable to those experienced three to four weeks post-injection of aflibercept protein. Further, in a laser-induced choroidal neovascularization model in NHPs, the industry standard model for testing new wet AMD therapies, we observed that a single intravitreal injection of ADVM-022 13 months before lasering provided the same level of protection from clinically relevant lesions as an intravitreal bolus of aflibercept at the time of lesioning, the current standard of care.

Long-term Aflibercept Expression in Aqueous and Vitreous Humor Following Intravitreal ADVM-022

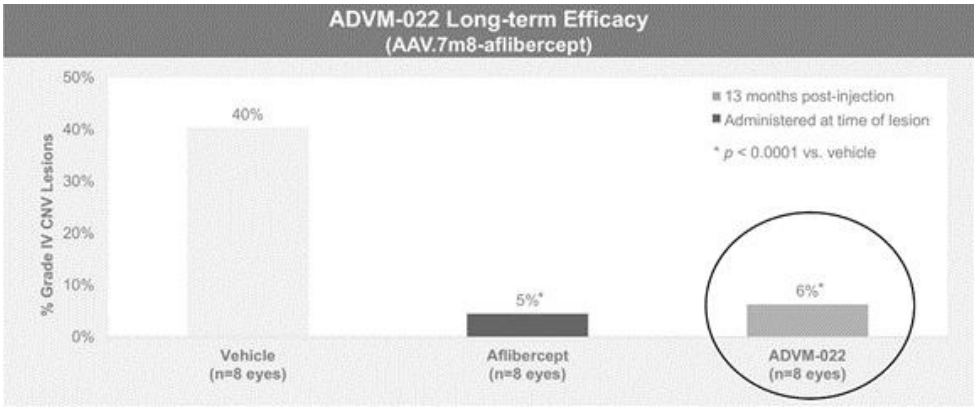


IVT=intravitreal; OS= oculus sinister; OD= oculus dextrus
Source: Angiogenesis, Exudation, and Degeneration Conference, February 2019.

Aflibercept Levels in the Retina ADVM-022 vs. Aflibercept Bolus (1.2 mg)



Source: Poster presentation, American Society of Gene and Cell Therapy (ASGCT) 21st Annual Meeting, May 2018



Source: Grishanin, et al. "Preclinical Evaluation of ADVM-022, a Novel Gene Therapy Approach to Treating Wet Age-Related Macular Degeneration." *Molecular Therapy.* 2018. DOI:https://doi.org/10.1016/j.ymthe.2018.11.003

Rare Diseases

Treatment of A1AT Deficiency

ADVM-043 is a gene therapy product candidate designed to provide stable, long-term A1AT protein expression for the treatment of A1AT deficiency. Preclinical studies in mice and non-human primates showed that ADVM-043 provided stable, robust, long-term expression of A1AT protein.

In December 2017 we began enrolling patients in the ADVANCE Phase 1/2 Clinical Trial of ADVM-043 for A1AT deficiency ("the ADVANCE trial"), a multi-center, open-label, dose-escalation study of ADVM-043 in patients with A1AT deficiency. The ADVANCE trial enrolled a total of six subjects, two subjects per dose at three doses of ADVM-043: 1.0×10^{12} vg/kg (8.0×10^{13} vg), 5.0×10^{12} vg/kg (4.0×10^{14} vg) and 1.5×10^{13} vg/kg (1.2×10^{15} vg). In November 2018, we announced preliminary data from the ADVANCE trial which demonstrate that ADVM-043 can be safely administered and was well tolerated during a mean follow-up period of 25 weeks post-administration at doses up to 1.5×10^{13} vg/kg (1.2×10^{15} vg). We observed at total of 15 adverse events (AEs), all of which were mild (Grade 1) in severity, except for one serious adverse event (SAE), which was considered Grade 3 in severity but found to be unrelated to ADVM-043. Of the 15 adverse events, only two were deemed possibly associated with

ADVM-043: Two AEs of elevated alanine aminotransferase ("ALT") (Grade 1, mild). The ALTs normalized within a few days after an increase in prednisone dose. However, A1AT protein expression did not reach a clinically meaningful level, nor was a dose response observed between the three cohorts.

Based on data from the ADVANCE trial, we discontinued the development of ADVM-043, and are conducting additional preclinical studies to evaluate potential paths forward for development of a product candidate for the treatment of A1AT deficiency.

We plan to provide an update on the A1AT deficiency program in the first half of 2019.

HAE

ADVM-053 is our preclinical gene therapy product candidate for the treatment of HAE. ADVM-053 is designed to be administered as a single IV injection to prevent HAE attacks. Like ADVM-043, ADVM-053 utilizes an AAVrh.10-based vector, which has been shown to target the liver, which is the natural source of C1EI. In 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. However, due to the lack of clinical efficacy that we observed in ADVM-043, also an AAVrh.10-based product candidate, are conducting additional preclinical studies to evaluate potential paths forward for development of a product candidate for the treatment of HAE.

We plan to provide an update on the ADVM-053 program in the first half of 2019.

Other Preclinical Product Candidates

In addition to our lead programs, we are currently utilizing our industry-leading development capabilities for our AAV-based directed evolution platform and are conducting observational studies. We are in the early stages of preclinical development for additional product candidates that we may advance in the future.

Partnered Program Product Candidates

Our partnered programs include vectors we are developing under collaboration agreements. Under an agreement with 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 provides for development of up to eight distinct ocular therapeutic targets, which includes AVA-311 for the treatment of juvenile X-Linked Retinoschisis ("XLRS").

We have also licensed to GenSight rights to use AAV.7m8 for GS030 gene therapy encoding channelrhodopsin protein. GenSight has received approval to initiate a Phase 1/2 trial in retinitis pigmentosa in the U.S., France, and U.K., which began in October 2018.

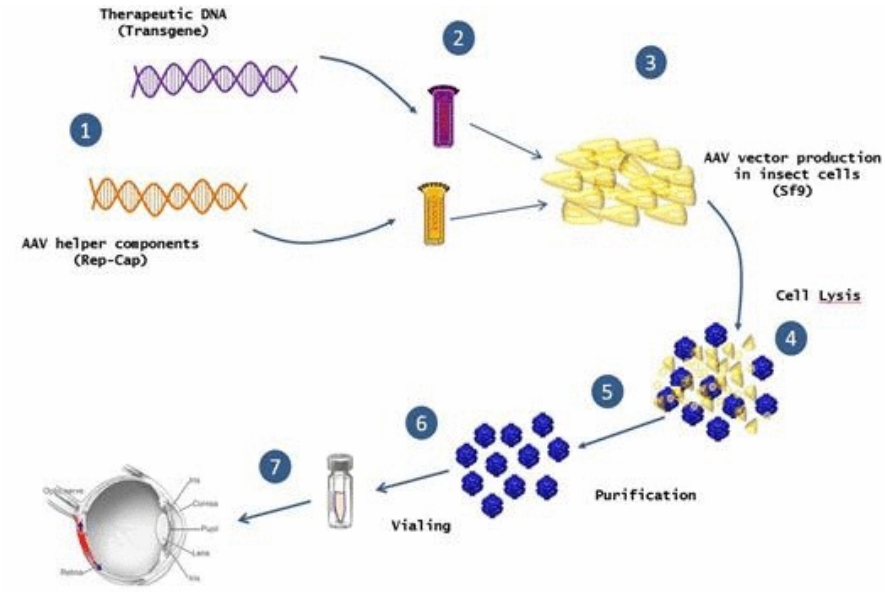
Manufacturing

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 is presented in the figure below, with the eye as an exemplary target organ.

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 vector replication.
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 buffer solution to lyse 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 wet AMD).

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 in humans.
- **High yield and low cost.** Because of its scalability, our BEVS system allows the production of large quantities of AAV vectors, up to the 2000-liter scale. Production at this scale lowers the unit cost of goods and may enable us to meet global demand for large markets, such as wet AMD.
- **High purity.** Our BEVS system coupled with our proprietary downstream purification process produces a highly pure drug substance.
- **Precedent regulatory framework.** Glybera, an AAV-based gene therapy, and several other vaccines and recombinant protein therapies have been approved by the FDA and EMA using a manufacturing process similar to our 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 with Lonza Houston, Inc. ("Lonza"). The license agreement provides that the parties will conduct activities to evaluate certain BEVS technology and that we may elect to engage Lonza to manufacture our products. We have 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 expand our in-house process development capabilities in stages, allowing us to develop larger-scale processes for transfer to our GMP contract manufacturers.

Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new proprietary technologies and therapies and a strong emphasis on intellectual property. We believe that our single administration, intravitreal approach to the treatment of wet AMD, our AAV-based directed evolution platform, and our expertise in the field of gene therapy provide us with

competitive advantages. However, we face actual or 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 wet AMD gene therapy ADVM-022 utilizes a proprietary vector and is administered through a single intravitreal injection and will compete with a variety of therapies currently marketed and in development, including biologics, small molecules and gene therapy. The key factors that contribute to success of any approved product include safety profile, efficacy, mode of administration and cost of goods. Existing anti-VEGF therapies are well-established therapies and are widely accepted by physicians, patients and third-party payers as the standard-of-care treatment of patients with wet AMD. 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 wet AMD, and we group them into four main categories:

- biosimilar anti-VEGFs (e.g. FYB201);
- combination / add-on therapy for efficacy improvement (e.g. faricimab);
- next generation anti-VEGF with quarterly injection (e.g. brolucizumab and abicipar pegol); and
- long acting delivery device / gene therapy to lower treatment frequency (e.g. ranibizumab port delivery system)

There are several other companies with marketed products or products in development for the treatment of wet AMD. These companies include Allergan, Bayer, Hoffmann-La Roche Ltd., Novartis, and Regeneron.

These companies, as well as competitors we may face, either alone or with their partners, for our other product candidates, 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.

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.

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 ocular 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, and endogenous molecules known to bind to and modulate such additional targets, in the research program, provided that Adverum is not currently developing that target.

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 amended and 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. In June 2018, we and Editas entered into a subsequent amendment to the agreement to extend the Research Period and First Option Exercise Date (each as defined in the collaboration, option, and license agreement with Editas, as amended).

Under the terms of the agreement, as amended, Editas had until November 2018 to exercise the option with respect to a designated initial indication, which Editas declined to do. With respect to the four other indications, Editas may exercise the option until August 2020, provided that the option will expire in August 2019 if Editas has not exercised one option with respect any other indication by such date. Upon Editas' timely exercise of the option with respect to 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 our 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

Gene Therapy for Eye Disease License Agreement: In May 2010, we entered into a license agreement, which was amended in September 2013, with the Regents of University of California ("Regents"). 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, 2018, 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.

This license agreement with the Regents continues in effect for the life of the last-to-expire patent, which we expect to occur in 2020. We expect the agreement to terminate prior to any commercialization of any product candidates to which they apply.

AAV.7m8 License Agreement: In June 2013, we entered into an exclusive worldwide sublicensable license agreement with the Regents to certain intellectual property related to improved AAV vectors, including the AAV.7m8 capsid. Under this license agreement, we are obligated to make certain de minimis license payments, certain milestone payments totaling up to $1.0 million upon reaching certain stages of development of the licensed products for a first 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. In addition, we are obligated to pay Regents royalties on sales of licensed products in the low single-digits, subject to adjustments and minimum thresholds.

Unless earlier terminated, this agreement will be in effect on a country-by-country, licensed product-by-licensed product basis until the expiration of the last claim of the licensed intellectual property covering the manufacture, use, or sale of such product in such country. We may terminate this agreement in whole or in party by giving Regents 30 days' prior written notice. Regents may terminate this agreement for 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

Cornell MSA

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 four 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 gene therapy programs directed to A1AT deficiency, HAE and severe allergy. Our license agreements with Cornell remained in effect despite termination of the MSA.

Following termination of the MSA we contracted with a large-scale CMO that complies with cGMP industry standards to produce product quantities for clinical trials and potential commercial supply.

Cornell License Agreements

In December 2015, Annapurna entered into three licensing agreements with Cornell, pursuant to which we have been 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. In October 2018, we notified Cornell of our intent to exercise our right to terminate the Allergy License Agreement, effective January 2019.

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.

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, we 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. We 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 us in a given country if we (i) before regulatory approval of a product in any country, have 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, have 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.

GenSight

On February 2014, we entered into an agreement with GenSight, in which we granted GenSight a non-exclusive license to our proprietary AAV.7m8 vector to develop gene therapy products to deliver certain therapeutic transgenes. Under the agreement, we are eligible to receive development, regulatory and commercial milestones. Also, we are eligible to receive low to mid-single digit royalties on sales of GenSight's licensed products.

GenSight is currently developing GS030, a gene therapy encoding channelrhodopsin protein which incorporates the AAV.7m8 capsid. GenSight has received approval to initiate a Phase 1/2 trial with GS030 to treat retinitis pigmentosa in the U.S., France, and the U.K., which began in October 2018.

Virovek

On October 12, 2011, we entered into an agreement with Virovek, Inc. ("Virovek"), in which we received a non-exclusive license to certain Virovek technology and know-how related to methods and materials for manufacturing AAV. Under the agreement, Virovek is entitled to certain license payments and low-single digit royalty payments. This license with Virovek continues in effect until expiration of the last-to-expire patent.

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. Additionally, we 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 100 patent applications pending in the U.S. and foreign jurisdictions, including more than 40 pending applications filed by or on behalf of universities which have granted us exclusive license rights to the technology. In addition, we own or license more than 30 issued patents that are currently in force. 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 patent families that are directed to AAV-based compositions and methods for treating or preventing eye diseases associated with neovascularization. Patents and applications in the first of these families relate to compositions and methods for the AAV-based delivery of anti-VEGF proteins, for use in treating neovascular diseases of the eye, including wet AMD, in patients who respond to anti-VEGF protein therapy. Patents in this family have issued in the U.S. and the Asia/Pacific region, and corresponding applications are pending in the U.S., elsewhere in North America, Europe, and Asia. Patents in this family 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 wet AMD using the AAV.7m8 vector to deliver ranibizumab or aflibercept. Each family has applications pending in the U.S. and corresponding applications pending abroad. 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 eight patent families that are directed to various aspects of our proprietary technology platform. One of these families contains issued patents in the US and Asia, and pending applications in the U.S., elsewhere in North America, Europe, and Asia. The remaining 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.

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 directed to improved rAAV virions that we have exclusively licensed in the ocular field includes granted patents in the U.S., as well as elsewhere in North America and Europe, as well as pending patent applications in the U.S. The patents in this family are projected to expire in 2024, subject to possible patent term extensions.

Another patent family directed to improved rAAV virions that we have exclusively licensed includes granted U.S. patents and a pending U.S. patent application that are expected to expire in 2031, subject to possible patent term extensions.

A third patent family that we have exclusively licensed includes claims directed to the novel AAV.7m8 vector, which allows delivery of transgenes to the retina via intravitreal injection, and which we utilize in our clinical candidate ADVM-022. This family includes issued patents in the U.S. 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 related to the Baculovirus/SF9 production system 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 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 exclusively licensed certain know-how related to gene therapy for A1AT deficiency and rights to an IND to perform clinical studies of gene therapy for A1AT.

Trade Secret Protection

In some circumstances we may rely on trade secrets to protect aspects of our technology and product candidates, including aspects for which we do not obtain patent protection. We seek to protect our trade secrets and confidential information, 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 confidential information 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

In the U.S., biologic products, including gene therapy products, are primarily regulated under the Federal Food, Drug, and Cosmetic Act ("FDCA") and the Public Health Service Act, as well as corresponding implementing regulations promulgated by the FDA. These laws and regulations govern, among other things, the testing, manufacturing, safety, purity, potency, efficacy, labeling, packaging, storage, record keeping, distribution, advertising-promotion, post-approval monitoring and reporting, sampling, export and import of biologics products. FDA clearance must be obtained before conducting human clinical testing of our gene therapy products. New biologics, as well as new dosage forms or new uses of previously approved biologics, require the submission of a BLA and approval by the FDA before being marketed in the U.S.

Within 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. FDA has published a growing body of guidance documents related to, among other things, gene therapy products developed for rare diseases, on patient-focused drug development, preclinical testing, and chemistry, manufacturing and controls, IND applications, and other areas of gene therapy development, all of which are intended to facilitate the industry's development of gene therapy products. Guidance documents provide the FDA's current thinking about a particular subject, but are not legally binding.

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

- Completion of non-clinical laboratory test and animal studies in accordance with current Good Laboratory Practice ("GLP"), regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- Submission of an IND to the FDA, which must become effective before human clinical trials may begin;
- Approval by the independent institutional review board ("IRB") of each clinical trial site before the trial may be initiated at that site;
- Approval by the institutional biosafety committee ("IBC") of each clinical trial site, which assesses the safety of clinical research and identifies any potential risks to public health or the environment;
- Performance of adequate and well-controlled human clinical trials according to Good Clinical Practice ("GCP") regulations, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the biologic product for its proposed indication;
- Establishment of the identity, strength, quality, purity or potency of the biologic product manufactured under cGMP;
- Satisfactory completion of an FDA inspection of each manufacturing facility at which the biologic product is produced, prior to commercialization, to assess compliance with cGMP, regulations, and any additional requirements pertaining to the manufacture and distribution of biologic products;
- Submission to 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;
- 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; application fees for products designated as orphan drugs by FDA as waived; and
- Compliance with any post-approval requirements or the potential to conduct post-approval studies.

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 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, and stability, 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.

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 FDA. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions relating to the content of the IND during the review period. In that case, the IND sponsor and the FDA must resolve any outstanding concerns before the IND goes into effect and the clinical trial begins. The FDA can 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 proceed without FDA authorization, and then only under terms authorized by FDA.

Clinical trials involve administering of the investigational biological product candidate to human subjects under the supervision of qualified investigators, who are 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 FDA as part of the IND. An independent IRB and IBC at each institution where the clinical trial will be conducted must also review and approve the plan for any clinical trial before it can begin at that institution, and the IRB must monitor the clinical trial until it is completed. The IBC will also assess the safety of the research and until it is completed. Clinical testing also must satisfy GCP requirements, including the requirements for informed consent from all subjects.

All clinical research performed in the United States in support of a BLA must be authorized in advance by the FDA as described above. However, a sponsor who wishes to conduct a clinical trial outside the U.S. 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, the FDA will accept a well-designed, well-conducted, non-IND foreign clinical trial as support for a BLA if (i) the clinical trial 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 clinical trial through an onsite inspection, if necessary. In addition, when an applicant submits data from a foreign clinical trial not conducted under an IND to support a BLA, FDA requires a description of the actions the applicant took to ensure that the research conformed to GCP. Further, additional requirements apply when a sponsor intends to base marketing approval of a new drug solely on foreign clinical data.

Clinical Trials

Clinical trials are typically conducted in three o sequential phases, which may overlap or be combined.

- In Phase 1, the typically biologic product candidate initially is introduced into a small number of healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early understanding of its effectiveness. In the case of some product candidates for severe or life-threatening diseases, especially when the product candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Phase 1 clinical trials of gene therapies are typically conducted in patients rather than healthy volunteers.
- Phase 2 clinical trials are typically well-controlled, closely monitored studies that are generally conducted in a larger subject population than Phase 1 trials to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and to preliminarily evaluate the efficacy of the product candidate for specific targeted indications. For Phase 2 clinical trials in gene therapy, although the subject population may be larger than the Phase 1 trials, the subject population may still remain relatively limited.
- Phase 3 clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the biological product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are generally undertaken with large numbers of subjects, 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 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.
- Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial approval. These clinical trials are used to gain additional data from treatment of patients in the intended therapeutic indication, particularly for long-term safety.

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 and the investigators for any serious and unexpected adverse events that occur during the study, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the clinical protocol or Investigator's Brochure, as well as any findings from other studies, tests in laboratory animals or

in vitro testing that suggest a significant risk for human subjects from the product candidate,. 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.

Human gene therapy products are a new category of therapeutics. As this is a relatively new and expanding areas of novel therapeutic interventions, there can be no assurance as to the length of the clinical trial period, the number of patients the FDA will require to be enrolled in the studies in order to establish the safety, efficacy, purity and potency of human gene therapy products, or that the data generated in these studies will be acceptable to FDA to support marketing approval. The FDA and the National Institutes of Health (NIH) developed a publicly accessible database, the Genetic Modification Clinical Research Information System, designed to facilitate safety reporting. The database includes information on gene transfer studies and serves as an electronic tool to facilitate the reporting and analysis of adverse events on these clinical trials.

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 CMC 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; 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, 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.

Each sponsor must register its clinical trials on the ClinicalTrials.gov website, the registry of new, on-going, and completed clinical trials of drugs, biologics, and device products.

Biologics License Applications

The results of preclinical studies and clinical trials, together with detailed 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 sufficiently complete to permit substantive review.

Under the Prescription Drug User Fee Act (“PDUFA”), 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 by issuing a complete response letter if the applicable statutory and regulatory criteria are not satisfied, and 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 the data differently than we interpret data. Moreover, even if a product receives approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited or subject to Risk Evaluation and Mitigation Strategies (REMS), 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. Even where a withdrawal is not required, the FDA still may seize existing inventory of such product or require a recall of product 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 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 the sponsor to develop additional data or conduct additional preclinical studies and clinical trials.

Before approving a BLA, the FDA will inspect the facilities at which the biologic is manufactured, and will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements. The FDA may also inspect the site(s) at which the clinical trials were conducted to assess their GCP compliance and will not approve the product unless compliance with the IND study requirements and GCP requirements is satisfactory.

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 FDA requests for additional information or clarification.

Once the FDA approves a BLA for a first indication, the biologic is granted 12 years of data exclusivity, meaning that no biosimilar application can be submitted to the FDA until four years after approval of the biologic, and no biosimilar application can be approved during the full 12-year period. These exclusivity provisions only apply to biosimilars—companies that rely on their own data and file a full BLA may be approved earlier than 12 years.

Expedited Development and Review Programs

The FDA has provided guidance to sponsors developing regenerative medicine therapies for serious or life-threatening diseases or conditions, with recommendations on the expedited development and review of these therapies, as provided under the FDCA and the 21st Century Cures Act.

Fast track designation. To qualify for fast track designation, a product candidate must be intended to treat a serious condition and address an unmet medical need. Advantages of fast track designation include the possibility for a rolling review, eligibility for priority review, and the ability to have greater interactions with the FDA. In addition, under the Fast Track program and FDA's accelerated approval regulations, the FDA may approve a biologic product based on a surrogate endpoint. A surrogate endpoint is a measurement of laboratory or clinical signs of a disease or conditions that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A biologic product candidate approved using a surrogate endpoint is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical trials to confirm the beneficial effect on a clinical endpoint. Failure to conduct or to confirm a clinical benefit during these required trials may result in FDA withdrawal of the approved biologic product from the market.

Any product submitted to the FDA for marketing approval, including under a Fast Track program, may be eligible for other types of FDA programs intended to expedite development and review, such as breakthrough therapy designation, regenerative medicine advanced therapy ("RMAT") designation, priority review designation, and accelerated approval.

Breakthrough therapy designation. To qualify for the breakthrough therapy program, a product candidate must be intended to treat a serious condition, and have preliminary clinical data indicating that it provides a substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient drug development program; intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review; and rolling review.

Regenerative medicine advanced therapy ("RMAT") designation. To qualify for the RMAT designation, a product candidate must be a regenerative medicine therapy intended to treat a serious condition, and there must be preliminary clinical evidence that the candidate has the potential to address unmet medical need. The FDA has indicated that gene therapies may qualify as regenerative medicine therapies. Advantages of RMAT designation include early interactions with FDA to discuss any potential surrogate or intermediate endpoints and the addresses potential ways to support accelerated approval and satisfy post-approval requirements.

Priority review. A product, including those that received fast track, breakthrough therapy, or RMAT designations, may be eligible for priority review, if it meets the criteria for priority review at the time the BLA is submitted. If priority review is granted, FDA has a 6-month goal for reviewing the marketing application or efficacy supplement

Accelerated approval. Drug or biologic products with evidence showing that they provide meaningful therapeutic benefit over existing treatments for serious or life-threatening illnesses may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of clinical data establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit. As a condition of approval, the FDA may require that a sponsor conduct post-marketing clinical trials.

Orphan Drug Designation ("ODD")

Under the Orphan Drug Act, the FDA may grant orphan drug designation to biological products intended to treat a rare disease or condition —-generally a disease or condition that affects fewer than 200,000 individuals in the United States, or if there is no reasonable expectation that the cost of developing and making the product available in the United States will be recovered from sales of the product.

ODD must be requested before submitting a BLA. ODD does not affect the regulatory review and approval process. However, the first BLA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA ODD is entitled to a seven-year exclusive marketing period in the United States for that product in the approved indication. During the seven-year marketing exclusivity period, the FDA may not approve any other applications to market a biological product containing the same active moiety for the same indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Among the other benefits of ODD are tax credits for certain research and a waiver of the BLA user fee.

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 manufacturers and their subcontractors are required to register their establishments with FDA and certain state agencies, and are subject to periodic unannounced inspections by 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, 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 biologic, 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 biologic. Failure to comply with these requirements can result in fines, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available biologics for uses that are not described in the product's labeling and that differ from those tested by the sponsor and approved by the FDA. Such off-label uses are common across medical specialties. However, if the FDA finds that we have promoted off-label use of any product that is eventually approved, 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, the pharmaceutical and biotechnology industry have received increased public and governmental scrutiny for 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 gene therapy products l. In the U.S. and other countries, sales of any products for which we receive marketing approval 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 or cell therapy products have been approved over the past several years by the FDA. Although the CMS subsequently approved its first method of coverage and reimbursement for Yescarta and Kymriah, 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 marketing applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in the Europe Union 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 products.

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.

Employees

As of February 28, 2019, we had 82 full-time employees, including a total of 14 employees with M.D. or Ph.D. degrees. Within our workforce, 60 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. 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, 2018, we had an accumulated deficit of $320.5 million. Losses have resulted principally from costs incurred in our research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, 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, cash equivalents, and short-term investments will be sufficient to fund our lead gene therapy programs into 2021. 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, 2018, our cash, cash equivalents and short-term investments were approximately $205.1 million. We currently expect this cash, cash equivalents and short-term investments to fund our planned operations and capital expenditures into 2021. 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 expected expenses to be incurred in connection with the build out of our new facility, 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 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 potentially to 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 our product candidates. If we are unable to develop, obtain regulatory approval for, or successfully commercialize, any or all of our product candidates, our business will be materially harmed.

Our product candidates are in the early stages of development and will require substantial preclinical and/or clinical development and testing, manufacturing process improvement and validation, bridging studies and regulatory approval prior to commercialization. It is critical to our business to successfully develop and ultimately obtain regulatory approval for one or more of these 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 product candidates;
- establishing commercial manufacturing capabilities, for example, by engaging third-party manufacturers that can provide products and services to support clinical development and the market demand for our product candidates, if approved;
- receipt of marketing approvals for any future products for which we complete clinical trials, including securing regulatory exclusivity to the extent available;
- successfully launching and commercial sales of the product, whether alone or in collaboration with potential partners;
- 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, obtaining, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates.

Our product candidate, ADVM-043 for the treatment of A1AT deficiency, failed to show sufficient efficacy in the ADVANCE trial, and was discontinued in 2018. For our lead gene therapy candidate, ADVM-022, we initiated the OPTIC trial in patients with wet AMD in the fourth quarter of 2018. For our rare disease programs, we are conducting additional preclinical studies to evaluate potential paths forward for development of a product candidate for these programs.

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 BLA to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market any of our 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 or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, any of our 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 have experienced or may 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 gene therapy products such as ours can be more expensive and take longer than for other product types, which are better known or more extensively studied to date. As an example, the FDA approved the first gene therapy product, LUXTURNA™ (voretigene neparvovec-rzyl) for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy in December 2017. The European Commission (EC) recently approved LUXTURNA™ for the treatment of vision loss due to a genetic mutation in both copies of the RPE65 gene and who have enough viable retinal cells.

Regulatory requirements governing gene and cell therapy products have changed and may continue to change in the future; such as the National Institutes of Health ("NIH") Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules and the modifications to the roles and responsibilities of the Recombinant DNA Advisory Committee ("RAC"). The FDA decides whether individual gene therapy protocols may proceed, and the FDA can put an IND on clinical hold.

Also, before a clinical trial can begin, that clinical site's IRB and IBC must review the proposed clinical trial to assess appropriateness to conduct the clinical trial at that site. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for human research on or for 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 studies, 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 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 lack efficacy, 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 may ultimately prove to be unsuccessful.

Few of our product candidates and proprietary viral vectors have been tested in clinical trials.

Drug development has inherent risk. Few of our product candidates and proprietary viral vectors have been evaluated in clinical trials in patients. Our lead product candidate, ADVM-022 for the treatment of wet AMD, uses a proprietary vector with an unknown safety profile in humans and may experience unexpected results in clinical trials in the future. Additionally, we decided to discontinue the development of product candidate ADVM-043 associated the ADVANCE trial, during the fourth quarter of 2018. Although ADVM-043 was safely administered and was well tolerated, A1AT protein measurements did not reach clinically meaningful levels of expression, and no dose response was observed between the first three cohorts of patients. We, or any licensee or development partner, will be required to demonstrate through adequate and well-controlled clinical trials that our product candidate or another party's product candidate containing one of our proprietary viral vectors are safe and effective for use in their target indications before seeking regulatory approvals for 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 or any clinical trials using our

proprietary viral vectors. Any such delay or failure could significantly harm our business prospects, financial condition and results of operations.

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 product candidates are not shown to be safe and effective, we may not realize the value of our investment in our technology. Promising preclinical results generated with a product candidate in animal models do not guarantee similar results when the candidate is tested in humans. For example, the levels of protein expression achieved from a vector in a preclinical model, including non-human primate ("NHP") models, may be significantly higher than the level of protein expression achieved in humans. In addition, even industry-accepted animal models may not accurately replicate human disease. For example, the laser-induced choroidal neovascularization model in NHP is the industry accepted animal model for wet AMD, where efficacy is assessed by reduction of the number of clinically relevant neovascular lesions. 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. Further, safety and/or efficacy issues with a product candidate may only become apparent when the candidate is tested in human patients suffering the relevant disease. For example, while pre-clinical testing of ADVM-043 showed promise, in the ADVANCE trial, A1AT protein did not reach a clinically meaningful level of expression and we decided to discontinue development of ADVM-043 in the fourth quarter of 2018. Furthermore, any future trials for any of our product candidates 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 marketing application and even fewer are approved for commercialization.

We cannot guarantee that results from any clinical trials that we plan will be successful, and any safety or efficacy 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 each clinical trial progresses.

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 changes in the final data compared to preliminary or 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 preclinical and clinical development, manufacturing, analytical testing, 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, analytical testing, or facilities of third-party manufacturers or testing laboratories 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 related products, including those already on the market, may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing our product candidates 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 patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Identifying and qualifying patients to participate in the OPTIC trial for ADVM-022 for the treatment of wet AMD and any future planned clinical trials will be critical to our success. The timing of current and future clinical trials will depend on the speed at which we can recruit patients to participate in future testing of these product candidates.

Patient 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 patients with wet AMD for the OPTIC trial for ADVM-022 and any future clinical trials for our product candidates. Potential patients may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our trials. Additionally, some patients may have neutralizing antibodies at titer levels that would prevent them from being enrolled in a clinical trial for any of our product candidates. The incidence of neutralizing antibodies in the population of patients, particularly for rare diseases, is unknown, and may be higher than we expect. As a consequence, enrollment in our clinical trials may be limited or slowed. We also may encounter difficulties in identifying and enrolling patients 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 patients, or those with required or desired characteristics to achieve diversity in a trial.

For our rare disease programs, these impact a small number of individuals in the U.S. (fewer than 200,000) and therefore there is a limited patient pool from which to draw for clinical trials. Enrollment of eligible patients with rare or orphan diseases may be limited or slower than we anticipate in light of the small patient 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 successfully conduct clinical trials if we cannot enroll a sufficient number of eligible patients 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 patients 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 patients, 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 into, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events. Although our vectors do not readily integrate into the patient's genome and is not known to cause disease in humans, our product candidates do use a viral vector delivery system. If patients negatively associate our product candidates with the adverse events caused by previous gene therapy products, they may not choose to enroll in our clinical trials, which would have a material adverse effect on our business and operations.

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, patients 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 discomfort 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, discomfort 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 one or more of our product candidates has side effects or causes serious or life-threatening side effects, the development of one or more of our product candidates may fail or be delayed, or, if one or more of our product candidates 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 transgene product, such as T-cell responses and/or antibodies against the expressed protein. For example, patients treated with ADVM-022 could develop antibodies against AAV.7m8 capsid and/or aflibercept protein. These antibodies could preclude these patients from receiving other AAV-based gene therapies and/or recombinant aflibercept protein in the future. Studies have also found that intravenous delivery of certain AAV vectors at very high doses may result in adverse events and prompted the recommendation that studies involving high doses of AAV vectors should be monitored carefully for such adverse events. In addition, patients given infusions of any protein may develop severe hypersensitivity reactions, infusion reactions, or serious side effects including transaminitis. 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, such as retinal detachment, endophthalmitis, ocular inflammation, cataract formation, glaucoma, hypotony, damage to the retina or cornea, and bleeding in 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.

Additionally, our lead product candidate, ADVM-022 is designed for long-term, sustained expression of an exogenous protein, aflibercept. Even though Eylea® (aflibercept) has been approved by several regulatory authorities, including the FDA, for the treatment of wet AMD, there may be side effects associated with aflibercept being expressed as a gene therapy treatment modality. If such side effects are serious or life-threatening, the development of our product candidate and future product candidates may fail or be delayed, or, if such product candidate(s) have received regulatory approval, such approval may be revoked, which would severely harm our business prospects, financial condition and results of operation.

Risks Related to Our Reliance on Third Parties

We will rely on third parties to conduct some preclinical testing and all clinical trials. If these third parties do not meet our deadlines or otherwise fail to 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 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 patients enrolled in our ongoing clinical trials unless we are able to transfer those patients 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 clinical trial, 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, product testing, protocol development, protocol performance, 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, product testing, protocol development, protocol performance, research, 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 not be successful at fulfilling their contractual obligations or may choose to 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. If any of these third parties on which we rely do not perform satisfactorily, we will remain responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the study plan and protocols, which we may not be able to do.

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. 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 some or 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 trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products.

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

We currently have relationships with a limited number of suppliers for the manufacturing and testing of our vector product candidates. Our suppliers may require licenses to manufacture or test 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, and may be unable to acquire such rights, to the extent that we do not already have them. All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract vendors for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in clinical trials must be manufactured and tested in accordance with 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 cGMP regulations enforced by the FDA through its facilities inspection program. Our contract manufacturers have not produced a commercially-approved AAV 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. If the facility does not pass a pre-approval plant inspection, FDA approval of the products will not be granted. 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.

Changes in laws and governmental policies may have an effect on regulations. For example, we and our contract vendors currently rely on other contractors based in the United Kingdom (UK). If the implementation of new governmental policies associated with BREXIT occurs, these governmental policies may affect our UK-based contractors' ability to comply with applicable regulations, including existing EU regulations. If they are unable to return to compliance, or if an acceptable substitute vendor cannot be identified, it may negatively impact our business. Further, to the extent that our UK-based contractors have supply relationships with vendors in the EU, these contractors may experience difficulties, delay or increased costs in receiving materials from their vendors in the EU, which could have a material adverse effect on our UK-based contractors' ability to provide the services or materials to us.

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 we become aware of a violation of our product specifications or applicable regulations, independent of 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 which may include the temporary or permanent suspension of a clinical trial 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 contractors fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new biologic product, revocation of a pre-existing approval, other civil or criminal penalties or closing one or more manufacturing or testing facilities. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if the service provided by an approved manufacturing or testing contractor is interrupted, there could be a significant disruption in commercial supply. An alternative contractor would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies showing comparability between approved product or testing, and product or testing provided after a contractor change, if a new manufacturing or testing contractor is relied upon for commercial production. Switching contractors 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, causing us to incur higher costs, and preventing 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 and other confidential information, which increases the possibility that a competitor will discover them or that our confidential information, including 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 confidential information, including 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 purposefully or inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Public disclosure of our confidential information also prevents us from seeking patent protection for that or related discoveries. 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 confidential information and 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 information or trade secrets from any such publication. However, we may fail to recognize or timely identify such confidential information or trade secrets prior to publication, and they may be disclosed. 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 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 provide timely data for our product candidates, it will delay our plans for our IND submissions and 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 or terminated for a number of reasons, including delays or terminations related to:

- the FDA failing to grant permission to proceed or placing the clinical trial on hold;
- patients failing to enroll or remain in our trial at the rate we expect;
- patients 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;
- patients 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 and 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 patients, 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 review and approval, 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 or terminated, 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 the credibility of our management team may be adversely affected 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 the credibility of our management team may be adversely affected 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 ongoing 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 obtain 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 wet AMD, A1AT deficiency, hereditary angioedema, 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 wet AMD 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 wet AMD, 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 wet AMD is smaller than we anticipate, we may not be able to achieve profitability and growth. Our projections of the number of people who have wet AMD, as well as the subset of people with the disease who have the potential to benefit from treatment with ADVM-022, 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 as we continue to enroll patients in the OPTIC trial of ADVM-022 for the treatment of wet AMD, and we cannot accurately predict the number of patients for whom treatment might be possible. For example, some patients with wet AMD have neutralizing antibodies at titer levels that may prevent them from benefiting from ADVM-022. If this patient population is larger than we estimate, the market for ADVM-022 may be smaller than we anticipate, and our future revenue may be adversely affected. Additionally, the potentially addressable patient population may be limited or may not be amenable to treatment with our product candidates for other reasons, 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 population for our rare disease programs is 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.

Our programs designed to treat rare genetic diseases may impact a small number of individuals (fewer than 200,000) in the U.S. Our estimates of both the number of people who have these rare genetic diseases, as well as the subset of people with these diseases who have the potential to benefit from our product candidates, may prove to be incorrect. The number of patients in the U.S. and elsewhere, or the portion of those patients who are amenable to treatment with our product candidates, may turn out to be lower than expected 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 any of our rare disease programs, because the potential target population is very small, we may never achieve profitability despite obtaining such significant market share.

Additionally, because the target patient population for any of our rare disease programs is 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 any of our product candidates targeting such rare disease will be adversely affected. The manner and level at which reimbursement is provided for services related to this product candidate (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 our product candidates targeting such rare disease.

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

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 cell and gene therapy products recently have been approved by the FDA. Although the U.S. Center for Medicare & Medicaid Services ("CMS") 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 Executive Orders and other directives designed to delay, circumvent or loosen the implementation of certain provisions of 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 22, 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. Moreover, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut

hole." Further, in July 2018, CMS announced that it has suspended further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program pending the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. 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 due to subsequent legislative changes to the statute, including the BBA, will stay in effect through 2027 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 and state 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, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. Although a number of these, and other potential, proposals will require authorization through additional legislation to become effective, 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 are increasingly passing legislation and implementing 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.
- We have to develop the manufacturing process for late stage clinical product, and our current process has not been fully characterized and therefore is open to potential variations that could lead to defective product or a product that does not meet specification.
- 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 strategic collaborations, which could adversely affect our ability to receive potential milestone and royalty payments.

We have entered into development or other strategic collaborations with major biotechnology or pharmaceutical companies. For example, we have entered into collaborations with Regeneron and Editas. 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. If we fail to maintain our current or future strategic collaborations, we may not realize milestone and royalty payments or other revenues under the collaboration agreements.

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, 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 patients 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, Lucentis® and EYLEA are currently available in the U.S. for treatment of wet AMD, diabetic macular edema, central retinal vein occlusion, and diabetic retinopathy. 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. For example, if we continue clinical development of, and seek to commercialize, ADVM-022 for the treatment of wet AMD, it will compete with a variety of therapies currently marketed and in development for wet AMD, using therapeutic modalities such as biologics, small molecules, long acting delivery devices, and gene therapy. Lucentis and EYLEA 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 wet AMD. There are several other companies with marketed products or products in development for the treatment of wet AMD, including Allergan, Bayer, Hoffmann-La Roche Ltd., Novartis, and Regeneron.

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. Trials using early versions of retroviral vectors, which integrate into, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events. Although none of our current product candidates utilize retroviruses and AAVs used in our product candidates have low-integrating potential and is not known to cause disease in humans, our product candidates do use a viral vector delivery system. The risk of serious adverse events 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 AAV serotypes to the ones we are using, even if not ultimately attributable to our product candidates or to an AAV serotype that we employ, 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. Similarly, our lead product candidate, ADVM-022 expresses aflibercept protein that is the same active therapy in Eylea. If safety or efficacy issues occur relating to Eylea, even if not ultimately attributable to aflibercept, this may negatively impact our product candidate. If any such adverse events or issues 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 clinical 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, clinical and scientific staff. The loss of service of any of our management or clinical or scientific staff 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, including a permanent Chief Medical Officer and a permanent Chief Financial Officer, 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 may not be able to attract or retain qualified management, 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. In addition, our current Chief Executive Officer is currently serving in a dual role as Chief Financial Officer, which may result in significant time constraints and burdens on performing each such role.

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 94 full-time employees as of December 31, 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 state 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 their exceptions and 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 exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions 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 exception 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 statutes governing healthcare fraud. 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

significant civil monetary penalties, for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. 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.

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 are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations (collectively, "Trade Laws"). We can face serious consequences for violations.

Among other matters, Trade Laws prohibit companies and their employees, agents, CRO's, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, provide, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else or anything of value to or from recipients in the public or private sector. Violations of Trade laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax assessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities to increase in time. We engage third parties for clinical trials and/or obtain necessary permits, licenses, registrations, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

If we fail to comply with applicable U.S. and foreign privacy and data protection laws and regulation, we may be subject to liabilities that adversely affect our business, operations and financial performance.

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention, and security of personal data, such as information that we collect about patients and healthcare providers in connection with clinical trials in the U.S. and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us to comply with federal, state, or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

For example, 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 health plans, healthcare clearinghouses and certain 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.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. Many countries in these regions have established or are in the process of establishing privacy and data security legal frameworks with which we, our customers, or our vendors must comply. For example, the EU has adopted the General Data Protection Regulation, or GDPR, which went into effect in May 2018 and introduced strict requirements for processing personal data. The GDPR is likely to increase compliance burden on us, including by mandating potentially burdensome documentation requirements, granting certain rights to individuals to control how we collect, use, disclose, retain and leverage information about them. The processing of sensitive personal data, such as physical health condition, may impose heightened compliance burdens under the GDPR and is a topic of active interest

among foreign regulators. In addition, the GDPR provides for breach reporting requirements, more robust regulatory enforcement and fines of up to 20 million euros or up to 4% of the annual global revenue. In the United States, California recently enacted the California Consumer Privacy Act ("CCPA"), which takes effect on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the U.S., which could increase our potential liability and adversely affect our business. Further, as we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

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, seizure of our products and 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. These applications and data encompass a wide variety of 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. 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.

We have entered into a new lease for a new corporate, process development, and research headquarters, which may be more costly to build out than we anticipate and may not provide all of the functionality we expect, which could cause us to incur unanticipated costs.

In June 2018, we entered into a lease for a building located in Redwood City, California, which we plan to occupy by year end 2019. This facility will serve as our new corporate headquarters and will include approximately 81,000 square feet of office, development, and research laboratory space. We believe this facility will enable us to increase our process development capabilities to the 1000-liter scale. There can be no assurance that the cost of building out this space will not be significantly more than we expect, or that the functionality of this space will be as we expect. Additionally, since we are not developing this space for clinical or commercial manufacturing production, we will continue to rely upon our limited number of suppliers to manufacture of our gene therapy products for clinical trials and if they are approved.

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 our code of conduct or regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct including code of conduct violations, 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.

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 false or 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.

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 term extensions for patents covering 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 product candidates of our programs.

We are aware of patent rights held by third parties that could be construed to cover certain aspects of our 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, we expect the relevant patent to expire before we 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 approval 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 seeking FDA approval, the development and ultimate sale of our 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. 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. Following December 31, 2019, unless we are no longer an accelerated filer, 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. 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, 2018, we cannot assure 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 ability to enroll and dose patients in any clinical trials that are on-going, or we that plan to conduct in the future;
- our ability to obtain regulatory approvals for our product candidates and delays or failure to obtain such approvals;
- our plans to conduct additional preclinical studies to determine the best gene therapy candidates in our rare disease programs to advance in development;
- 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 have been subject to securities class action lawsuits in the past, and could be subject to additional such lawsuits in the future, which could result in substantial losses and may divert management's time and attention from our business.

In the past, we and certain of our former officers were involved in purported securities class action lawsuits, which have since been settled. The purported securities class action lawsuits asserted that the defendants violated the Securities Exchange Act of 1934, as amended, and the Securities Act of 1933, as amended, and alleged that the defendants who are no longer at Adverum 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 program which has been discontinued, and the prospects of AVA-101. We settled these lawsuits for $13.0 million, of which $1.0 million we contributed to cover our indemnification obligations to the underwriters, and the remainder was contributed by our insurers. Any future litigation of this type could result in payment of damages or settlement fees and diversion of management's attention and resources, any of 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. 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 $22.5 million. Further, pursuant to the 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 $64.5 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, and will continue to be an emerging growth company until December 31, 2019. We are also a smaller reporting company. 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. Even after we no longer qualify as an emerging growth company, we may continue to be a "smaller reporting company," which would allow us to continue take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the 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.

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, 2018, we had U.S. federal net operating loss ("NOL") carryforwards of approximately $100.0 million to offset future federal income. Approximately $57.0 million of NOLs expire at various years beginning with 2036. As of December 31, 2018, we also had U.S. state NOL carryforwards of approximately $61.1 million to offset future state income. U.S. State NOLs expire at various years beginning with 2036. At December 31, 2018, we also had approximately $65.0 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 for approximately $43.0 million 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 and research and developments tax credits for both federal and state purposes were severely limited and therefore we removed a significant amount of NOLs and research and development tax credits 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.

On June 28, 2018, we entered into a lease on a new facility, which will serve as our new corporate headquarters. The new facility is located in Redwood City, California with approximately 81,000 square feet of office, laboratory, and process development space, which we believe is adequate for our current needs. We expect to occupy the new facility by year end 2019. The term of the lease is ten years and also provides for two options to extend the lease term for a period of seven years each.

Item 3. Legal Proceedings

Not applicable.

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 is listed on the Nasdaq Global Market under the symbol "ADVM".

Holder of Record

As of February 28, 2019, we had approximately 14 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.

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 discontinued development of AVA-101, and so we did 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 trial, 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 and clinical studies, including the clinical development of our wet AMD gene therapy, ADVM-022, and the preclinical studies for our rare disease programs. We have used all of the $106.5 million of net proceeds from the IPO for the purposes described in the registration statement, as revised in this paragraph.

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, 2018 and 2017 and as of December 31, 2018 and 2017, from our consolidated financial statements, which are included elsewhere in this Annual Report on Form 10-K. We derived the consolidated financial data for the years ended December 31, 2016, 2015 and 2014, and as of December 31, 2016, 2015, and 2014, 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.

(In thousands, except per share data)	Years ended December 31, 2018	2017	2016	2015	2014
Consolidated Statements of Operations and Comprehensive Loss Data:					
Revenue					
Collaboration and license revenue	$ 1,612	$ 1,849	$ 1,455	$ 2,319	$ 572
Operating expenses:					
Research and development (1)	50,133	39,839	31,670	25,462	16,976
General and administrative (2)	24,560	20,857	24,355	22,107	7,998
Impairment of goodwill and intangible assets (3)	5,000	—	60,714	—	—
Restructuring charges (4)	—	—	—	2,573	—
Total operating expenses	79,693	60,696	116,739	50,142	24,974
Operating loss	(78,081)	(58,847)	(115,284)	(47,823)	(24,402)
Other income (expense)					
Interest expense	—	—	—	—	(18)
Other income (expense), net	4,204	2,700	762	370	(21)
Changes in fair value of warrant liabilities	—	—	—	—	(759)
Loss on extinguishment of related-party convertible notes	—	—	—	—	(204)
Total other income (expense), net	4,204	2,700	762	370	(1,002)
Net loss before income tax benefit	(73,877)	(56,147)	(114,522)	(47,453)	(25,404)
Income tax benefit (5)	1,250	—	775	—	—
Net loss after income tax benefit	(72,627)	(56,147)	(113,747)	(47,453)	(25,404)
Deemed dividend (6)	—	—	—	—	(3,230)
Net loss attributable to common stockholders	$ (72,627)	$ (56,147)	$ (113,747)	$ (47,453)	$ (28,634)
Other comprehensive loss:					
Net unrealized loss on marketable securities	168	(182)	6	(6)	—
Foreign currency translation adjustment	(4)	(774)	(2)	(15)	(17)
Comprehensive loss	$ (72,463)	$ (57,103)	$ (113,743)	$ (47,474)	$ (25,421)
Net loss per share attributable to common stockholders-basic and diluted	$ (1.18)	$ (1.29)	$ (3.14)	$ (1.86)	$ (2.46)
Weighted-average common shares outstanding-basic and diluted	61,375	43,661	36,246	25,479	11,651

(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. During the year ended December 31, 2018, we recorded approximately $3.8 million of one-time stock-based compensation expense in connection with the separation agreement with a certain executive officer.

(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. During the year ended December 31, 2018, we recorded an impairment charge of $5.0 million on in-process research and development assets related to our intangible assets.

(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.

(In thousands)	As of December 31, 2018	2017	2016	2015	2014
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 154,949	$ 70,519	$ 222,170	$ 221,348	$ 159,404
Short-term investments	50,130	119,966	—	37,732	—
Working capital	198,035	183,067	215,378	254,418	154,807
Total assets	213,495	201,905	234,583	264,319	161,906
Other non-current liabilities	243	481	386	—	—
Accumulated deficit	(320,543)	(254,062)	(197,915)	(84,168)	(36,715)
Total stockholders' equity	201,167	184,028	215,600	252,592	149,483

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 need in ocular and rare diseases. We develop gene therapy product candidates designed to provide durable efficacy by inducing sustained expression of a therapeutic protein. Our core capabilities include clinical development, novel vector discovery, and in-house manufacturing expertise, specifically in scalable process development, assay development, and cGMP quality control.

We are advancing our lead gene therapy product candidate ADVM-022 for the treatment of wet age-related macular degeneration ("wet AMD"). In September 2018, we received Fast Track designation for ADVM-022 for the treatment of wet AMD from the U.S. Food and Drug Administration ("FDA").

Our IND application for ADVM-022 for the treatment of wet AMD became active in August 2018. We initiated the Phase 1 OPTIC trial for ADVM-022 in patients with wet AMD, dosing our first subject in November 2018. The OPTIC trial is designed to be a multi-center, open-label, Phase 1, dose-escalation safety trial in patients with wet AMD who have demonstrated responsiveness to anti-VEGF treatment. The OPTIC trial is expected to enroll 18 patients to evaluate three doses of ADVM-022 administered as a single intravitreal injection. We expect to provide an update on enrollment from the OPTIC trial in the first half of 2019. In addition, we expect to provide interim data from the OPTIC trial by the first quarter of 2020. Additionally, we are evaluating whether other ocular diseases with approved anti-VEGF therapies might also be treated with ADVM-022.

We have been developing ADVM-043, an investigational gene therapy candidate for the treatment of alpha-1 antitrypsin ("A1AT") deficiency. In December 2017 we began enrolling patients in the ADVANCE trial, a multi-center, open-label, dose-escalation study of ADVM-043 in patients with A1AT deficiency. In November 2018, we announced preliminary data from the ADVANCE trial, which showed that ADVM-043 was safe and well tolerated at the doses tested, but A1AT protein expression did not reach a clinically meaningful level, nor was a dose response observed between the three cohorts. Based on data from the ADVANCE trial, we discontinued the development of ADVM-043 and are conducting additional preclinical studies to evaluate potential paths forward for development of a product candidate for the treatment of A1AT deficiency. We plan to provide an update on this program in the first half of 2019.

We have also been developing ADVM-053, our preclinical gene therapy product candidate for the treatment of hereditary angioedema ("HAE"). However, due to the lack of clinical efficacy that we observed in ADVM-043, we are reviewing the results from the ADVANCE trial to inform further development of gene therapy candidates for the treatment of systemic rare diseases, including ADVM-053 for the treatment of HAE, and are conducting additional preclinical studies to evaluate potential paths forward for development of a product candidate for the treatment of HAE. We plan to provide an update on this program in the first half of 2019.

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 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.

In June 2018 we signed a lease with an initial 10-year term for a new facility in Redwood City, California which we plan to occupy by year end 2019. This facility will serve as our new corporate headquarters and will include approximately 81,000 square feet of office, laboratory, and process development space. We believe this facility will enable us to increase our process development capabilities to the 1000-liter scale.

Financial Overview

Summary

We have not generated positive cash flow or net income from operations since our inception and, as of December 31, 2018, we had an accumulated deficit of $320.5 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 trial 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 2*, Summary of significant accounting policies—Revenue Recognition – Collaboration and License Revenue,* of the notes to consolidated financial statements included in this Form 10-K for details. We have no clinical or commercial manufacturing facilities, and contract out all of our clinical manufacturing activities 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.

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, after issuance costs. Since then, during the year ended December 31, 2018, we sold no additional shares under the 2017 stock offering agreement. Under the 2017 stock offering agreement, we have sold a total of 6,550,232 shares of our common stock at market prices, raising total net proceeds of $22.5 million, after 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.

As of December 31, 2018, we had $205.1 million in cash, cash equivalents and short-term investments. We currently expect this cash, cash equivalents and short-term investments to fund our planned operations and capital expenditures into 2021.

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, 2018, we had no deferred revenue related to collaboration arrangements with our strategic partners . We recognized $1.6 million and $1.8 million of revenue associated with these collaboration arrangements during the years ended December 31, 2018 and 2017, 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. In June 2018, we and Editas entered into a subsequent amendment to the agreement to extend the Research Period and First Option Exercise Date (each as defined in the collaboration, option, and license agreement with Editas, as amended). Under the terms of the agreement, Editas had until November 2018 to exercise one option, which Editas declined to do. Editas has until August 2020 to exercise additional options, provided that

they exercise at least one option by August 2019. Refer to Note 6 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 AMD 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.

Agreement with GenSight

In February 2014, we entered into an agreement with GenSight, in which we granted GenSight a non-exclusive license to our proprietary AAV.7m8 vector to develop gene therapy products to deliver certain therapeutic transgenes. Under the agreement, we are eligible to receive development, regulatory and commercial milestones. Also, we are eligible to receive low to mid-single digit royalties on sales of GenSight's licensed products.

During the year ended December 31, 2018, GenSight achieved a clinical development milestone pursuant to the agreement. This milestone was previously constrained under Topic 606. We earned a $0.2 million milestone payment, which we recognized as revenue in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018.

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 trial 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.

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, regulatory, and investor relations functions associated with being a public reporting company.

Impairment of Goodwill and Intangible Assets

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.

In the third quarter of 2018, we identified an impairment indicator related to the intangible asset and performed an impairment analysis. On October 30, 2018, we decided to discontinue the development of ADVM-043. We recorded an impairment charge of $5.0 million on IPR&D assets related to our intangible asset for ADVM-043. We recorded this amount in Impairment of intangible assets on our consolidated statements of operations and comprehensive loss.

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. We base our estimates 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

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.

Effective January 1, 2018, we adopted Accounting Standard Update ("ASU") No. 2014-09, Revenue from Contracts with Customers ("Topic 606") using the modified retrospective approach. Our collaboration agreements with Regeneron, Editas and GenSight were impacted by the adoption of the new revenue standards under Topic 606. We present the results for reporting periods beginning after January 1, 2018 under Topic 606, while prior period results are not adjusted and continue to be reported in accordance with the revenue standards under Topic 605.

Upon adoption of Topic 606, we recorded a net decrease of $6.1 million to our deferred revenue and opening accumulated deficit as of January 1, 2018 for the cumulative effect of the adoption. The effect of the adoption is summarized for our license and collaboration agreements as follows:

Collaboration Agreement with Regeneron—Under Topic 606, we determined the transaction price at contract inception to be $8.0 million, which was related to the non-refundable upfront payment for license and research services. The arrangement also provides for additional payments to us when we achieve certain development and regulatory milestones. Because these milestone payments are not within our control and we do not consider them probable of being achieved until the events occur, we did not include them in the transaction price at contract inception. We allocated the transaction price of $8.0 million at contract inception to two performance obligations. Our deferred revenue associated with Regeneron collaboration agreement as of December 31, 2017 under Topic 605 was $6.5 million. As a result of adopting Topic 606, we recorded a $6.5 million reduction to our deferred revenue and

opening accumulated deficit during the three months ended March 31, 2018 as the performance obligations associated with the Regeneron deferred revenue were satisfied as of January 1, 2018. There was no outstanding deferred revenue associated with Regeneron as of December 31, 2018.

Collaboration Agreement with Editas— Under Topic 606, the transaction price is $1.5 million related to the $1.0 million non-refundable upfront payment for license and research services at contract inception and the one-time, non-refundable cash payment of $0.5 million made by Editas in February 2018 in consideration for extending the agreement. The arrangement provides for additional payments to us when we achieve certain development and regulatory milestones. Because these milestone payments are not within our control and we do not consider them probable of being achieved until the events occur, we did not include them in the transaction price. We allocated the transaction price of $1.5 million to a single performance obligation, research and development. Our deferred revenue associated with Editas collaboration agreement as of December 31, 2017 under Topic 605 was $0.5 million. As a result of adopting Topic 606, we recorded an increase of $0.4 million to our deferred revenue and opening accumulated deficit during the three months ended March 31, 2018 due to differences in the timing of recognition under Topic 606.

During the year ended December 31, 2018, we recognized revenue of $1.4 million, associated with the Editas collaboration agreement. There was no outstanding deferred revenue associated with Editas as of December 31, 2018.

License Agreement with GenSight— On February 2014, we entered into an agreement with GenSight, where we granted GenSight a non-exclusive license to our proprietary AAV.7m8 vector. Under the agreement, we are eligible to receive development, regulatory and commercial milestones. Also, we are eligible to receive low to mid-single digit royalties on sales of GenSight's licensed products.

During the year ended December 31, 2018, GenSight achieved a clinical development milestone pursuant to the agreement. This milestone was previously constrained under Topic 606. We earned a $0.2 million milestone payment, which we recognized as revenue in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018.

Under Topic 605, our revenue for the year ended December 31, 2018 would have been $2.2 million.

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, 2018 and 2017, 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. 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. We generally recognize the grant date fair value of the stock-based awards on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. We recognize stock-based compensation expense related to awards to non-employees 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 our employee stock purchase plan. 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. We base the expected term for non-employee awards 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. We base the risk-free interest rate 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, we write down long-lived assets to their respective fair value based on discounted cash flows. Significant management judgment is required in the forecast of future operating results that we use 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 we consider 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 we consider the asset indefinite-lived, we test it 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. We record impairment loss 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, we would deem the associated IPR&D asset definite-lived and would then amortize it based on its estimated useful life at that point in time based on respective patent term and test it for impairment only when impairment indicators are present as discussed above under
long-lived assets.

Income Tax

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, 2018 and 2017 of approximately $47.3 million and $35.5 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, 2018, we had U.S. federal net operating loss ("NOL") carryforwards of approximately $100.0 million to offset future federal income. Approximately $57.0 million of NOLs expire at various years beginning with 2036. As of December 31, 2018, we also had U.S. state NOL carryforwards of approximately $61.1 million to offset future state income. U.S. State NOLs expire at various years beginning with 2036. At December 31, 2018, we also had approximately $65.0 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 and research and development tax credits for both federal and state purposes are severely limited and therefore we removed a significant amount NOL and research and development tax credits 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. We have not recognized any interest and penalties related to income taxes in the consolidated statements of operations and comprehensive loss during the years ended December 31, 2018 and 2017.

Recent Accounting Standard Update

In February 2016, the Financial Accounting Standards Board ("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. We adopted the new standard using the modified retrospective approach as of January 1, 2019 and expect to record a lease liability in the range of $24.0 million to $27.0 million, and a right-to-use asset of approximately $23.0 million and $26.0 million, and no adjustment to the accumulated deficit. While we continue to evaluate the effect of the standard, we anticipate that the adoption will result in a material increase in assets and liabilities on our consolidated balance sheet and will not have a material impact on the consolidated statement of operations or statement of cash flows.

In June 2018, the FASB issued ASU 2018-07, "Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting" that expands the scope of ASC Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of ASC Topic 718 to nonemployee awards except for certain exemptions specified in the amendment. The guidance is effective for fiscal years beginning after December 15, 2018, including interim reporting periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. We are currently evaluating the impact of the guidance on our consolidated financial statements.

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 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 provide less extensive disclosure about our executive compensation arrangements; and
- we do not require stockholder non-binding advisory votes on executive compensation or golden parachute arrangements.

We will remain an "emerging growth company" until December 31, 2019.

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

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

	Years ended December 31,		
	2018	2017	Increase/(Decrease)
	(In thousands)		
Collaboration and license revenue	$ 1,612	$ 1,849	$ (237)
Operating expenses:			
Research and development	50,133	39,839	10,294
General and administrative	24,560	20,857	3,703
Impairment of goodwill and intangible assets	5,000	—	5,000
Total operating expenses	79,693	60,696	18,997
Operating loss	(78,081)	(58,847)	(19,234)
Other income (expense), net	4,204	2,700	1,504
Net loss before income tax benefit	(73,877)	(56,147)	(17,730)
Income tax benefit	1,250	—	1,250
Net loss	$ (72,627)	$ (56,147)	$ (16,480)

Revenue

Our revenue for the year ended December 31, 2018 related to research services under our collaboration agreement with Editas and milestone payment under the license agreement with GenSight while our revenue for the year ended December 31, 2017 related to license and research services under our collaboration agreements with Regeneron and Editas. We recognized our collaboration and license revenue for the year ended December 31, 2018 under Topic 606, which we adopted effective January 1, 2018. We recognized our collaboration and license revenue for the year ended December 31, 2017 under Topic 605. Under Topic 605, our revenue for the year ended December 31, 2018 would have been $2.2 million.

Research and Development Expense

Research and development expense increased to $50.1 million for the year ended December 31, 2018, from $39.8 million for the year ended December 31, 2017. This increase was primarily due to an overall increase in research and development activity, including $4.3 million of higher costs associated with the ADVANCE trial for ADVM-043 for A1AT deficiency and start-up activities for the OPTIC trial for ADVM-022 for the treatment of wet AMD, $1.5 million of higher material production costs related to our wet AMD and rare disease programs to support clinical trials, $1.3 million of higher outside research and development services and $4.0 million in higher compensation and benefits.

We expect that research and development expenses will increase in future periods as we continue to invest in advancing our gene therapy product candidate, ADVM-022 and earlier-stage research programs.

General and Administrative Expense

General and administrative expense increased to $24.6 million for the year ended December 31, 2018, from $20.9 million for the year ended December 31, 2017. The increase in general and administrative expense was primarily due to $5.8 million in severance-related expenses, predominantly stock-based compensation expenses as a result of the modification of the vesting and exercisability of stock awards associated with the departure of our previous chief executive officer, and $0.4 million in increased compensation costs, and $0.3 million increase in rent expense, partially offset by $3.1 million lower legal expenses as the year ended December 31, 2017 included settlement costs associated with the securities class action lawsuit and $2.0 million for the termination of our master service agreement with Cornell.

We expect that general and administrative expenses will increase in future periods as we continue to support advancing our gene therapy programs. We anticipate increased expenses related to audit, legal, regulatory, and investor relations functions associated with being a public reporting company.

Goodwill and Intangible Assets Impairment Charge

During the year ended December 31, 2018, we identified an impairment indicator related to the intangible asset for ADVM-043 and performed an impairment analysis. In November 2018, we announced our decision to discontinue the development of ADVM-043. We recorded an impairment charge of $5.0 million on IPR&D assets related to our intangible asset for ADVM-043. There were no impairment charges during the year ended December 31, 2017.

Other Income, Net

The increase in other income, net was primarily due to higher interest income from our investments in marketable securities as we invested in higher yield securities, as well as higher average invested balances.

Income Tax Benefit

In connection with our impairment charge, we derecognized a deferred tax liability of $1.3 million related to the intangible asset for ADVM-043. There was no income tax benefit during the year ended December 31, 2017.

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, 2018, we had an accumulated deficit of $320.5 million. As of December 31, 2018, we had $205.1 million in cash, cash equivalents and short-term investments. We believe that our existing cash, cash equivalents, and short-term investments as of December 31, 2018 will be sufficient to fund our planned operations and capital expenditures into 2021.

In August 2017, we entered into our 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. During the year ended December 31, 2018, we sold no additional shares under the 2017 stock offering agreement. 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 $64.5 million, after discounts and other issuance costs.

In June 2018, we entered into a lease for a facility located in Redwood City, California, that will serve as our new corporate headquarters and will include approximately 81,000 square feet of office, manufacturing, and laboratory space. We believe this facility will enable us to expand our manufacturing process development activities at 1000-liter scale.

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, and capital expenditures related to the build out of our new facility. At this time, we cannot reasonably estimate the nature, timing or aggregate amount of costs for our development, potential commercialization, and internal research and development programs. However, 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. 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 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,	
	2018	2017
	(In thousands)	
Net cash (used in) provided by:		
Operating activities	$ (53,964)	$ (45,421)
Investing activities	69,444	(122,204)
Financing activities	69,949	16,748
Effect of changes in foreign currency exchange rates	—	(774)
Net increase (decrease) in cash and cash equivalents and restricted cash	$ 85,429	$ (151,651)

Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2018 was $54.0 million, primarily as a result of the net loss of $72.6 million mainly driven by our continued research and development activities, partially offset by $20.3 million of non-cash

charges mainly related to stock-based compensation expense, impairment of intangible asset and depreciation and amortization expense, and $1.6 million of net decrease in operating assets and liabilities.

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.

Cash (Used in) Provided by Investing Activities

Net cash provided by investing activities was $69.4 million for the year ended December 31, 2018 consisted of $149.0 million resulting from the maturities of marketable securities, partially offset by $78.7 million of purchases of marketable securities and $0.8 million of purchases of property and equipment. Purchases of property and equipment primarily consisted of the acquisition of laboratory equipment to support our research and development 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.

Cash Provided by Financing Activities

Net cash provided by financing activities for year ended December 31, 2018 consisted of $70.2 million of the net proceeds from the sales of our common stock, primarily our underwritten public offering of our common stock in February in which we raised net proceeds of $64.5 million, $1.0 million of the proceeds from the exercises of stock options and employee stock purchases and $0.1 million of the proceeds from our financing arrangement with the Alpha-1 Project, Inc., partially offset by $1.0 million in taxes paid relating to net share settlement of restricted stock units and $0.2 million repayment of our Banque Publique d'Investissement ("BPI France") loan.

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.

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

Under SEC rules and regulations, as a smaller reporting company, we are not required to provide the information required by this item. See Item 6, Selected Financial Data above.

Item 8. Financial Statements and Supplementary Data.

ADVERUM BIOTECHNOLOGIES, INC.
CONSOLIDATED FINANCIAL STATEMENTS
AS OF DECEMBER 31, 2018AND 2017
AND FOR THE YEARS ENDED DECEMBER 31, 2018 AND 2017

Index

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Adverum Biotechnologies, Inc. (the "Company") as of December 31, 2018, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the year then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018, and the results of its operations and its cash flows for the year then ended, in conformity with U.S. generally accepted accounting principles.

Adoption of Topic 606

As discussed in Note 2 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), using the modified retrospective method effective January 1, 2018.

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 audit. 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 audit 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 audit, 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 audit 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 audit 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 audit provides a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.

San Jose, California
March 6, 2019

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 sheet of Adverum Biotechnologies, Inc. and its subsidiaries (the "Company") as of December 31, 2017, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for the year 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 the results of its operations and its cash flows for the year 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 began serving as the Company's auditor in 2013. In 2018 we became the predecessor auditor.

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

	As of December 31,	
	2018	2017
Assets		
Current assets:		
Cash and cash equivalents	$ 154,949	$ 70,519
Short-term investments	50,130	119,966
Prepaid expenses and other current assets	3,675	3,256
Total current assets	208,754	193,741
Property and equipment, net	3,586	3,024
Restricted cash	999	—
Deposit and other non-current assets	156	140
Intangible asset	—	5,000
Total assets	$ 213,495	$ 201,905
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,707	$ 1,731
Accrued expenses and other current liabilities	8,784	6,964
Deferred rent, current portion	228	129
Deferred revenue, current portion	—	1,850
Total current liabilities	10,719	10,674
Long-term liabilities:		
Deferred rent, net of current portion	1,366	222
Deferred revenue, net of current portion	—	5,250
Deferred tax liability, non-current	—	1,250
Other non-current liabilities	243	481
Total liabilities	12,328	17,877
Commitments and contingencies (Note 10)		
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, 2018 and 2017; 62,965,468 and 49,015,339 shares issued and outstanding at December 31, 2018 and 2017, respectively	6	5
Additional paid-in capital	522,503	439,048
Accumulated other comprehensive loss	(799)	(963)
Accumulated deficit	(320,543)	(254,062)
Total stockholders' equity	201,167	184,028
Total liabilities and stockholders' equity	$ 213,495	$ 201,905

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,	
	2018	2017
Collaboration and license revenue	$ 1,612	$ 1,849
Operating expenses:		
Research and development	50,133	39,839
General and administrative	24,560	20,857
Impairment of goodwill and intangible assets	5,000	—
Total operating expenses	79,693	60,696
Operating loss	(78,081)	(58,847)
Other income:		
Other income, net	4,204	2,700
Net loss before income taxes	(73,877)	(56,147)
Income tax benefit	1,250	—
Net loss	$ (72,627)	$ (56,147)
Other comprehensive loss:		
Net unrealized gain (loss) on marketable securities	168	(182)
Foreign currency translation adjustment	(4)	(774)
Comprehensive loss	$ (72,463)	$ (57,103)
Net loss per share - basic and diluted	$ (1.18)	$ (1.29)
Weighted-average common shares outstanding-basic and diluted	61,375	43,661

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 $0.0001 PAR VALUE		ADDITIONAL PAID-IN	ACCUMULATED OTHER COMPREHENSIVE	ACCUMULATED	TOTAL STOCKHOLDERS'
	Shares	Amount	CAPITAL	INCOME (LOSS)	DEFICIT	EQUITY
Balance at December 31, 2016	**41,805,009**	**$ 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**
Issuance of common stock, net of issuance costs of $4,140	11,642,128	1	70,186	—	—	70,187
Adoption of Topic 606	—	—	—	—	6,146	6,146
Stock-based compensation expense	—	—	13,432	—	—	13,432
Common stock issued upon exercise of stock options	1,606,137	—	688	—	—	688
Common stock issued under employee stock purchase plan	120,475	—	340	—	—	340
Common stock issued upon release of restricted stock units	773,965	—	—	—	—	—
Restricted stock surrendered for taxes	(192,576)	—	(1,191)	—	—	(1,191)
Net unrealized loss on marketable securities	—	—	—	168	—	168
Foreign currency translation adjustments	—	—	—	(4)	—	(4)
Net loss	—	—	—	—	(72,627)	(72,627)
Balance at December 31, 2018	**62,965,468**	**$ 6**	**$ 522,503**	**$ (799)**	**$ (320,543)**	**$ 201,167**

See accompanying notes to consolidated financial statements.

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

	Years ended December 31,	
	2018	2017
Cash flows from operating activities:		
Net loss	$ (72,627)	$ (56,147)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	1,750	2,096
Stock-based compensation expense	13,432	8,723
Amortization of premium on marketable securities	24	593
Accreted interest on BPI	95	—
Impairment of goodwill and intangible assets	5,000	—
Non-cash research and development expense	—	60
Other	(17)	10
Changes in operating assets and liabilities:		
Accounts receivable, net	—	886
Prepaid expenses and other current assets	(793)	(491)
Deposit and other long-term assets	(16)	—
Accounts payable	(67)	333
Accrued expenses and other current liabilities	215	487
Restructuring liabilities	—	(25)
Deferred revenue	(953)	(1,849)
Deferred rent	1,243	(97)
Deferred tax liability	(1,250)	—
Net cash used in operating activities	(53,964)	(45,421)
Cash flows from investing activities:		
Purchases of marketable securities	(78,726)	(209,787)
Sales of marketable securities	—	1,003
Maturities of marketable securities	148,979	87,596
Purchases of property and equipment	(809)	(1,016)
Net cash provided by (used in) provided by investing activities	69,444	(122,204)
Cash flows from financing activities:		
Proceeds from offering of common stock, net of issuance costs	70,187	16,519
Proceeds from issuance of common stock pursuant to option exercises	688	367
Taxes paid related to net share settlement of restricted stock units	(1,191)	(313)
Proceeds from employee stock purchase plan	340	175
Repayment of BPI loan	(175)	—
Proceeds from a financing arrangement	100	—
Net cash provided by financing activities	69,949	16,748
Effect of foreign currency exchange rate on cash and cash equivalents	—	(774)
Net increase (decrease) in cash and cash equivalents and restricted cash	85,429	(151,651)
Cash and cash equivalents and restricted cash at beginning of period	70,519	222,170
Cash and cash equivalents and restricted cash at end of period	$ 155,948	$ 70,519
Supplemental schedule of noncash investing and financing information		
Fixed assets in accounts payable and current liabilities	$ 1,616	$ 115

See accompanying notes to consolidated financial statements.

ADVERUM BIOTECHNOLOGIES, INC.

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 and is headquartered in Menlo Park, California. The Company is a clinical-stage gene therapy company targeting unmet medical need in ocular and rare diseases. The Company develops 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, novel vector discovery, and in-house manufacturing expertise, specifically in scalable process development, assay development, and current Good Manufacturing Practices ("cGMP") quality control. Adverum is advancing a pipeline of gene therapy product candidates designed to treat wet age-related macular degeneration ("AMD") as well as rare diseases. 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 $320.5 million as of December 31, 2018. 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 into 2021.

In May 2016, the Company completed the acquisition of all of 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.

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 May 11, 2016 under the ticker symbol "AAVL," commenced trading on The Nasdaq Global Market under the ticker symbol "ADVM" on May 12, 2016.

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.

Restricted Cash—Restricted cash primarily consists of cash collateral to letter of credit provided to the landlord in relation to a lease agreement (see Note 10).

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. There were no impairment indicators noted for the Company's amortizable long-lived assets, fixed assets, in the year ended December 31, 2017.

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, 2018, the Company recorded an impairment charge of $5.0 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 elected to account for this financial liability at fair value and recorded as other non-current liabilities in its consolidated balance sheets (see Note 5). The 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.

Effective January 1, 2018, the Company adopted the new revenue standards under Topic 606 using the modified retrospective approach. Results for reporting periods beginning after January 1, 2018 are presented under Topic 606, while prior period results are not adjusted and continue to be reported in accordance with the revenue standards under Topic 605. Under Topic 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company's license and collaboration arrangements with Regeneron Pharmaceuticals, Inc. ("Regeneron"), Editas Medicine, Inc. ("Editas"), and GenSight Biologics ("GenSight") are within the scope of Topic 606.

Upon the adoption of Topic 606, the Company recorded a net decrease of $6.1 million to its deferred revenue and opening accumulated deficit as of January 1, 2018 for the cumulative effect of the adoption. The effect of the adoption is summarized for the Company's license and collaboration agreements as follows:

Collaboration and License Revenue

Collaboration Agreement with Regeneron—Under Topic 606, the transaction price at contract inception was determined to be $8.0 million, which was related to the non-refundable upfront payment for license and research services. The arrangement also provides for additional payments to the Company when certain development and regulatory milestones are achieved. Because these milestone payments are not within the control of the Company and are not considered probable of being achieved until the events occur, the Company did not include them in the transaction price at contract inception. The transaction price of $8.0 million at contract inception was allocated to two performance obligations. The Company's deferred revenue associated with its Regeneron collaboration agreement as of December 31, 2017 under Topic 605 was $6.5 million. As a result of adopting Topic 606, the Company recorded a $6.5 million reduction to its deferred revenue and opening accumulated deficit during the three months ended March 31, 2018 as the performance obligations associated with the Regeneron deferred revenue were satisfied as of January 1, 2018. There was no outstanding deferred revenue associated with Regeneron as of March 31, 2018 or December 31, 2018.

Collaboration Agreement with Editas—Under Topic 606, the transaction price at contract inception was determined to be $1.0 million, which was related to the non-refundable upfront payment for license and research services. The arrangement provides for additional payments to the Company when certain development and regulatory milestones are achieved. Because these milestone payments are not within the control of the Company and are not considered probable of being achieved until the events occur, the Company did not include them in the transaction price at contract inception. The transaction price of $1.0 million at contract inception was allocated to a single performance obligation. The Company's deferred revenue associated with its Editas collaboration agreement as of December 31, 2017 under Topic 605 was $0.5 million. As a result of adopting Topic 606, the Company recorded an increase of $0.4 million to its deferred revenue and opening accumulated deficit during the three months ended March 31, 2018 due to differences in the timing of recognition under Topic 606.

During the year ended December 31, 2018, the Company recognized revenue of $1.4 million associated with the Editas collaboration agreement. There was no outstanding deferred revenue associated with Editas as of December 31, 2018.

License Agreement with GenSight— On February 2014, the Company entered into an agreement with GenSight, where the Company granted GenSight a non-exclusive license to its proprietary AAV.7m8 vector. Under the agreement, the Company is eligible to receive development, regulatory and commercial milestones. Also, the Company is eligible to receive low to mid-single digit royalties on sales of GenSight's licensed products.

During the year ended December 31, 2018, GenSight achieved a clinical development milestone pursuant to the agreement. This milestone was previously constrained under Topic 606. The Company earned a $0.2 million milestone payment, which was recognized as revenue in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2018.

Under Topic 605, the Company's revenue for the year ended December 31, 2018 would have been $2.2 million.

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 trial 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.

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 5 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.

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 12 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, 2018 and 2017, 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 comprises 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, 2018 and 2017.

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 February 2016, the Financial Accounting Standards Board ("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. We adopted the new standard using the modified retrospective approach as of January 1, 2019 and expect to record a lease liability in the range of $24.0 million to $27.0 million, and a right-to-use asset of approximately $23.0 million to $26.0 million, and no adjustment to the accumulated deficit. While the Company continues to evaluate the effect of the standard, the Company anticipates that the adoption will result in a material increase in assets and liabilities on its consolidated balance sheet and will not have a material impact on the consolidated statement of operations or statement of cash flows.

In June 2018, the FASB issued ASU 2018-07, "Compensation – Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting" that expands the scope of ASC Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of ASC Topic 718 to nonemployee awards except for certain exemptions specified in the amendment. The guidance is effective for fiscal years beginning after December 15, 2018, including interim reporting periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. The Company is currently evaluating the impact of the guidance on its consolidated financial statements.

3. Impairment Evaluation for Goodwill and Intangible Assets

The Company recorded In-process Research and Development ("IPR&D") intangible assets upon the acquisition of Annapurna in May 2016. The carrying value of the IPR&D intangible asset was $5.0 million as of June 30, 2018. The Company evaluates indefinite lived intangible assets for impairment on an annual basis or more frequently if indicators of impairment exist. 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 year ended December 31, 2018, the Company identified an impairment indicator related to the intangible asset and performed an impairment analysis. On October 30, 2018, the Company decided to discontinue the development of ADVM-043. The Company recorded an impairment charge of $5.0 million on IPR&D assets related to the Company's intangible asset for ADVM-043. This amount was recorded in Impairment of intangible assets on the Company's consolidated statements of operations and comprehensive loss.

4. 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, 2018	Amortized Cost Basis	Unrealized Gains	Unrealized Loses	Estimated Fair Value
Money market funds	$ 126	$ —	$ —	$ 126
U.S. government and agency securities	25,792	1	(4)	25,789
Commercial paper	147,606	—	—	147,606
Corporate bonds	27,778	5	(17)	27,766
Certificates of deposit	1,420	—	—	1,420
Total cash equivalents and short-term investments	202,722	6	(21)	202,707
Less: Cash equivalents	(152,577)	—	—	(152,577)
Total short-term investments	$ 50,145	$ 6	$ (21)	$ 50,130
December 31, 2017				
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

Management determined that the gross unrealized losses on the Company's marketable securities as of December 31, 2018 were temporary in nature. Therefore, none of the Company's marketable securities were other-than-temporarily impaired as of December 31, 2018.

All investments as at December 31, 2018 have a remaining maturity of one year or less.

5. 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.

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, 2018 and 2017.

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):

December 31, 2018	Total Carrying Value	Quoted Prices In Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Money market funds	$ 126	$ 126	$ —	$ —
U.S. government and agency securities	25,792	—	25,792	—
Commercial paper	147,606	—	147,606	—
Corporate bonds	27,778	—	27,778	—
Certificates of deposit	1,420	—	1,420	—
Total cash equivalents and short-term investments	$ 202,722	$ 126	$ 202,596	$ —
Other noncurrent liability:				
Financing arrangement	$ —	$ —	$ —	$ —
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

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 $0 and approximately $0.2 million was outstanding as of December 31, 2018 and 2017, respectively (see Note 9). 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, 2018 and 2017. 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 TAP financing liability was remeasured to $0 due to the Company's decision to discontinue the A1AT program during the year ended December 31, 2018.

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.

6. Significant Agreements

Editas —In January 2018, the Company entered into an agreement to amend its collaboration, option and license agreement with Editas. The Company originally entered into an agreement with Editas in August 2016 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. 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. In June 2018, the Company and Editas entered into a subsequent amendment to the agreement to extend the Research Period and First Option Exercise Date (each as defined in the collaboration, option, and license agreement with Editas, as amended).

Under the terms of the agreement, as amended, Editas had until November 2018 to exercise the option with respect to a designated initial indication, which Editas declined to do. With respect to the four other indications, Editas may exercise the option until August 2020, provided that the option will expire in August 2019 if Editas has not exercised one option with respect to any other indication by such date. Upon Editas' timely exercise of the option with respect to 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 our 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.

Under Topic 606, the transaction price is $1.5 million related to the $1.0 million non-refundable upfront payment for license and research services at contract inception and the one-time, non-refundable cash payment of $0.5 million made by Editas in February 2018 in consideration for extending the agreement. The arrangement provides for additional payments to the Company when certain development and regulatory milestones are achieved. Because these milestone payments are not within the control of the Company and are not considered probable of being achieved until the events occur, the Company did not include them in the transaction price. The transaction price of $1.5 million was allocated to a single performance obligation, research and development services.

During the year ended December 31, 2018, the Company recognized revenue of $1.4 million associated with the Editas collaboration agreement. The Company had no deferred revenue balance as of December 31, 2018.

7. Property and Equipment, Net

Property and equipment, net consists of the following:

	December 31,	
	2018	2017
	(In thousands)	
Computer equipment and software	$ 646	$ 535
Laboratory equipment	5,470	4,956
Furniture and fixtures	678	552
Leasehold improvements	1,602	1,549
Construction in progress	1,612	105
Total property and equipment	10,008	7,697
Less accumulated depreciation and amortization	(6,422)	(4,673)
Property and equipment, net	$ 3,586	$ 3,024

Depreciation and amortization expense related to property and equipment was $1.8 million and $2.1 million for the years ended December 31, 2018 and 2017, respectively.

8. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consist of the following:

	December 31,	
	2018	2017
	(In thousands)	
Compensation expense	$ 2,944	$ 2,259
Accrued preclinical costs	289	1,255
Accrued professional fees	2,291	2,295
Accrued clinical and process development costs	1,561	910
Other	1,699	245
Total accrued expenses and other current liabilities	$ 8,784	$ 6,964

9. 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, 2018, the total carrying value, which approximates the fair value, of the conditional advance was $0.3 million, of which $0.2 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. As of December 31, 2017, 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 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 "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 5.

The following table presents the TAP financing activity:

	Years ended December 31,	
	2018	2017
	(In thousands)	
Balance of TAP financing liability as of the beginning of the year (1)	$ 157	$ 74
Funding (2)	—	100
Gain on fair value of TAP financing liability (3)	(157)	(17)
Balance of TAP financing liability as of the end of the year	$ —	$ 157

(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 in the Company's consolidated balance sheet and other income, net in the Company consolidated statement of operations and comprehensive loss.

10. Commitments and Contingencies

Facility Lease Agreement

On June 28, 2018, the Company entered into a lease on a new facility with office, laboratory, and manufacturing space, which will serve as the Company's new corporate headquarters. The term of the lease is ten years and also provides for two options to extend the lease term for a period of seven years each. The Company is obligated to make lease payments totaling approximately $49.3 million over the initial term of the lease.

Under the lease, the Company will receive a tenant improvement allowance for the costs associated with the design, development and construction of tenant improvements for the leased facility. The Company has provided the landlord with a letter of credit in the amount of $1.0 million. The security for the letter of credit of $1.0 million is classified as restricted cash under long term assets on the balance sheet.

The Company leases its Menlo Park 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, 2018, future minimum commitments under the Company's facility operating leases were as follows:

Years ended December 31,	Future Commitments
	(In thousands)
2019	$ 3,344
2020	4,221
2021	4,683
2022	4,846
2023	5,016
Thereafter	28,837
Total minimum lease payments	$ 50,947

Rent expense recognized under the operating lease, including additional rent charges for utilities, parking, maintenance, and real estate taxes was $3.3 million and $1.8 million for the years ended December 31, 2018 and 2017, respectively.

Contractual Obligations

As of December 31, 2018, the Company had a contractual obligation of approximately $0.7 million for a contract manufacturing with a vendor for materials production related to 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, 2018, 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 fees payments were approximately $0.1 million and $0.5 million for each of the years ended December 31, 2018, and 2017.

The Company was a party to a master services 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 the Company to pay Cornell $13.3 million ratably over four years for these services as services were performed. 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 the termination of the MSA, the Company 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 gene therapy programs directed to A1AT deficiency, HAE and severe allergy. The Company's license agreements with Cornell remained in effect despite the termination of the MSA.

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, 2018 and 2017.

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 asserted claims under the Securities Exchange Act of 1934, as amended (the "Exchange Act") and Securities Act of 1933, as amended (the "Securities Act") and alleged that the defendants who are no longer with the Company 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 sought 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 alleged that, in connection with the Company's follow-on stock offering, the same 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 sought unspecified compensatory and rescissory damages, attorneys' fees and other costs. The plaintiff has dismissed the two institutional stockholder defendants.

In March 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 was contributed by the Company to cover its indemnification obligations to the underwriters, and the remainder was 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. In January 2018, the San Mateo Superior Court entered a judgment and order finally approving the settlement. On February 5, 2018, the U.S. District Court entered an order dismissing the consolidated federal action with prejudice. 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.

11. 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 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 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 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 9), 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 other non-current liabilities and additional paid-in capital in the Company's consolidated balance sheet for the year ended December 31, 2016.

12. 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, 2018, a total of 19,353,469 shares of common stock were reserved for issuance and 2,695,347 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
Granted	2,049	5.94		
Exercised	(1,606)	0.43		
Cancelled/forfeited	(691)	5.90		
Balance at December 31, 2018	6,447	$ 5.83	7.6	$ 3,594
Vested and expected to vest as of December 31, 2018	6,447	$ 5.83	7.6	$ 3,594
Exercisable at December 31, 2018	3,321	$ 6.63	6.7	$ 2,630

(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 $3.15 per share as of December 31, 2018.

In June 2017, the Company granted 150,000 stock options outside the Plans to its certain executive officers.

The total intrinsic value of stock options exercised during the years ended December 31, 2018 and 2017 were $8.2 million and $4.8 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,	
	2018	2017	2018	2017
Expected volatility	80%	82%	78%	52%
Expected term (in years)	6.0	6.0	0.5	0.5
Expected dividend yield	—	—	—	—
Risk-free interest rate	2.8%	1.9%	2.3%	1.3%

The weighted-average fair values of options granted during the years ended December 31, 2018 and 2017, were $4.15 and $1.99, respectively.

As of December 31, 2018, there was $6.5 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,	
	2018	2017
Expected volatility	77%	84%
Expected term (in years)	7.7	8.8
Expected dividend yield	—	—
Risk-free interest rate	2.7%	2.3%

As of December 31, 2018, unrecognized stock-based compensation expense related to unvested non-employees stock options was approximately $0.1 million, which is expected to be recognized over a weighted-average period of 1.1 years, based on the estimated fair value at December 31, 2018.

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
Granted	1,381	5.94	
Vested and released	(774)	(3.46)	
Forfeited	(725)	(4.28)	
Balance at December 31, 2018	2,397	$ 9.23	4.8

The weighted-average grant-date fair value of RSUs granted during the years ended December 31, 2018 and 2017, were $5.94 and $2.81, respectively. During the years ended December 31, 2018 and 2017, total fair value of RSUs vested was $2.7 million and $2.0 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, 2018, there was $7.4 million of unrecognized compensation cost related to unvested RSUs that is expected to be recognized over a weighted-average period of 2.5 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, 2018, 120,475 shares were issued under the ESPP. As of December 31, 2018, a total

of 1,331,773 shares of common stock were available for future issuance under the ESPP. As of December 31, 2018, 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,	
	2018	2017
	(In thousands)	
Research and development	$ 4,820	$ 5,253
General and administrative	8,612	3,470
Total share-based compensation expense	$ 13,432	$ 8,723

During the year ended December 31, 2018, the Company recorded approximately $4.1 million of stock-based compensation expense as a result of the modification of the vesting and exercisability of stock awards associated with the departure of two of its executives.

13. 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, 2018 and 2017 was $0.4 million and $0.3 million, respectively.

14. Income Taxes

The Company recorded $1.3 million income tax benefit related to the change in the deferred tax liabilities balance due to intangible assets impairment recognized in the third quarter of 2018 and no income tax benefit or expense were recorded for the year ended December 31, 2017.

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

	Years ended December 31,	
	2018	2017
	(In thousands)	
U.S.	$ (45,024)	$ (36,923)
Foreign	(28,853)	(19,224)
Loss before income taxes	$ (73,877)	$ (56,147)

A reconciliation of income tax expense computed at the statutory federal income tax rate of 21% and 34% during the year ended December 31, 2018 and 2017, respectively, to income taxes as reflected in the financial statements is as follows:

	Years ended December 31,	
	2018	2017
	(In thousands)	
Federal income tax expense at statutory rate	$ (15,514)	$ (19,090)
Non-deductible foreign research expenses	—	19
Stock compensation	(1,512)	(76)
Non-deductible expenses	75	61
Other	41	—
Research and development tax credits	(1,215)	(507)
Change in valuation allowance	11,219	7,935
Foreign rate differential	(586)	1,495
Rate change	—	10,163
Change in uncertain tax positions	6,242	—
Total tax benefit	$ (1,250)	$ —

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,	
	2018	2017
	(In thousands)	
Deferred tax assets:		
Net operating loss carryforwards	$ 37,247	$ 27,142
Accruals, reserve and other	827	2,586
Stock-based compensation	4,549	3,623
Tax credit carryforwards	4,161	1,774
Property and equipment	310	274
Intangibles	38	64
Other	122	—
Total deferred tax assets before valuation allowance	47,254	35,463
Valuation allowance	(47,254)	(35,463)
Total deferred tax assets	—	—
Deferred tax liabilities:		
IPR&D	—	(1,250)
Total deferred tax liabilities	$ —	$ (1,250)
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 fully offset by its valuation allowance.

On December 22, 2017 the SEC staff issued SAB 118, which allowed the Company to record provisional amounts during a measurement period not to extend beyond one year of the enactment date. 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. In accordance with SAB 118, the Company has completed its analysis during the fourth quarter of 2018 noting no material adjustments from the provisional amounts recorded in the prior year. In addition, the guidance indicates that either accounting for deferred taxes related to GILTI or to treat any taxes on future GILTI inclusions as period cost are both acceptable methods subject to an accounting policy election. The Company has elected to treat future GILTI inclusions if any as period costs.

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, 2018 and 2017. The valuation allowance increased approximately $11.8 million and $12.0 million during the years ended December 31, 2018 and 2017, respectively.

As of December 31, 2018, the Company had U.S. federal net operating losses ("NOLs") carryforwards of approximately $100.0 million to offset any future federal income. Approximately $57.0 million of NOLs expire at various years beginning with 2036. As of December 31, 2018, the Company also had U.S. state NOL carryforwards of approximately $61.1 million to offset any future state income. U.S. state NOLs expire at various years beginning with 2036. At December 31, 2018, the Company also had approximately $65.0 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, 2018, the Company had federal research and development tax credit carryforwards of approximately $3.2 million available to reduce future tax liabilities which expire at various years beginning with 2036. As of December 31, 2018, the Company had state credit carryforwards of approximately $3.3 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 development 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. Federal, 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, 2013 through December 31, 2018. 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, 2018 and 2017 of approximately $8.8 million and $2.7 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,	
	2018	2017
	(In thousands)	
Unrecognized tax benefits as of the beginning of the year	$ 2,745	$ 2,157
Increase (decrease) related to prior year tax provisions	1,941	—
Increase related to current year tax provisions	4,119	588
Unrecognized tax benefits as of the end of the year	$ 8,805	$ 2,745

The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2018, and 2017, 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.

15. 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,	
	2018	2017
	(In thousands)	
Stock options	6,447	6,695
Restricted stock units	2,397	2,515
ESPP	62	71
Warrants to purchase common stock	90	90
	8,996	9,371

16. 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, 2018	June 30, 2018	September 30, 2018	December 31, 2018
	(In thousands, except per share amounts)			
Revenue	$ 216	$ 493	$ 833	$ 70
Total operating expenses (1)	(18,162)	(20,396)	(24,306)	(16,829)
Net loss	(17,200)	(18,810)	(20,958)	(15,659)
Basic and diluted net loss per share	$ (0.30)	$ (0.30)	$ (0.34)	$ (0.25)

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)

(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 10). 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.

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 Ms. Patterson, 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, 2018. 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, 2018, 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, 2018, 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, 2018. 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, 2018 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 concluded that, as of December 31, 2018, 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 2019 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, 2018, 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:

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†	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	
10.2†	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	
10.3†	A1AT Deficiency License Agreement between Annapurna Therapeutics Limited and Cornell University, dated December 15, 2015.	001-36579	10-Q	August 9, 2016	10.4	
10.4†	HAE License Agreement between Annapurna Therapeutics Limited and Cornell University, dated December 15, 2015.	001-36579	10-Q	August 9, 2016	10.5	
10.5†	Allergy License Agreement between Annapurna Therapeutics Limited and Cornell University, dated December 15, 2015.	001-36579	10-Q	August 9, 2016	10.6	
10.6†	License Agreement between AAVLife and Inserm Transfert, dated July 4, 2014.	001-36579	10-Q	August 9, 2016	10.9	
10.7†	Amendment No. 1 to License Agreement between AAVLife and Inserm Transfert, dated October 5, 2015.	001-36579	10-Q	August 9, 2016	10.10	
10.8†	Collaboration, Option and License Agreement with Editas Medicine, Inc., dated August 8, 2016.	001-36579	10-Q	November 8, 2016	10.1	
10.9†	Amendment to Collaboration, Option and License Agreement with Editas Medicine, Inc., dated January 25, 2018.	001-36579	10-K	March 6, 2018	10.10	
10.10(#)	Avalanche Biotechnologies, Inc. Amended and Restated 2006 Equity Incentive Plan.	333-197133	S-1	June 30, 2014	10.4	
10.11(#)	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	
10.12(#)	Adverum Biotechnologies, Inc. 2014 Equity Incentive Award Plan, as amended and restated.					X

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
10.13(#)	Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan.	333-197133	10-K	March 6, 2018	10.14	
10.14(#)	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	
10.15(#)	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2014 Equity Incentive Award Plan.	001-36579	10-K	March 6, 2018	10.16	
10.16(#)	Adverum Biotechnologies, Inc. 2014 Employee Stock Purchase Plan, as amended and restated.					X
10.17(#)	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	
10.18(#)	Offer Letter, dated November 19, 2015, by and between Avalanche Biotechnologies, Inc. and Paul Cleveland.	001-36579	8-K	November 20, 2015	10.1	
10.19(#)	Offer Letter, dated January 29, 2016, by and between Avalanche Biotechnologies, Inc. and Amber Salzman.	001-36579	8-K	February 1, 2016	10.2	
10.20(#)	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	
10.21(#)	Offer Letter, dated June 10, 2016, by and between Adverum Biotechnologies, Inc. and Leone Patterson	001-36579	8-K	June 13, 2016	10.1	
10.22(#)	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	
10.23(#)	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	
10.24(#)	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	
10.25(#)	Offer Letter, dated May 4, 2015, by and between Avalanche Biotechnologies, Inc. and Jennifer Cheng, Ph.D.	001-36579	10-K	March 6, 2018	10.30	
10.26	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	
10.27	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	
10.28	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	
10.29(#)	Form of Indemnification Agreement for directors and executive officers.	333-197133	S-1/A	July 18, 2014	10.12	
10.30(#)	2012 Change in Control Benefit Plan.	333-197133	S-1/A	July 18, 2014	10.13	
10.31(#)	Form of Change in Control Severance Agreement for executive officers other than the chief executive officer.	001-36579	10-K	March 6, 2018	10.36	
10.32(#)	Amendment to the Change in Control and Severance Agreement for Mehdi Gasmi.					X

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
10.33(#)	Form of Inducement Stock Option Agreement.	001-36579	8-K	November 20, 2015	10.3	
10.34(#)	2017 Inducement Plan, as amended and restated.					X
10.35(#)	Form of Stock Option Grant Notice and Option Agreement under the 2017 Inducement Plan.	333-220894	S-8	October 11, 2017	99.2	
10.36(#)	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	
10.37	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	
10.38	Release Agreement, dated as of October 3, 2017, by and between the Company and Steven Schwartz, M.D.	001-36579	10-K	March 8, 2018	10.43	
10.39(#)	June 2018 Compensation Actions with Interim Chief Executive Officer and Chief Science and Technology Officer	001-36579	8-K	June 15, 2018	Item 5.02	
10.40	Lease dated as of June 28, 2018, between Adverum Biotechnologies, Inc. and HCP LS Redwood City, LLC	001-36579	10-Q	August 8, 2018	10.2	
10.41	June 5, 2018, amendment to Editas Agreement.	001-36579	10-Q	August 8, 2018	10.3	
10.42(#)	Non-Employee Director Compensation Arrangements	001-36579	10-Q	August 8, 2018	10.4	
10.43(#)	Amber Salzman Separation Agreement	001-36579	10-Q	November 8, 2018	10.1	
10.44(#)	Athena Countouriotis Separation Agreement	001-36579	10-Q	November 8, 2018	10.2	
10.45(#)	Change in Compensation of Leone Patterson in connection with promotion to Chief Executive Officer	001-36579	8-K	October 24, 2018	Item 5.02	
10.46†	Exclusive License Agreement, between the Company and the Regents of the University of California ("UC"), dated June 17, 2013 (the "UC License")					X
10.47†	License Agreement, between the Company and Virovek, Inc. ("Virovek"), dated October 12, 2011 (the "Virovek License")					X
10.48(#)	Amended and Restated Offer Letter with Leone Patterson, dated October 24, 2018					X
10.49(#)	Change in Control and Severance Agreement with Leone Patterson, dated October 24, 2018					X
21.1	List of subsidiaries	001-36579	10-K	March 6, 2018	21.1	
23.1	Consent of Deloitte & Touche LLP Independent Registered Public Accounting Firm					X
23.2	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

EXHIBIT NUMBER	EXHIBIT DESCRIPTION	INCORPORATED BY REFERENCE				PROVIDED HEREWITH
		FILE NUMBER	FORM	DATE	EXHIBIT NUMBER	
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
101.INS	XBRL Instance Document.					X
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.

Item 16. Form 10-K Summary

None.

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, 2019

ADVERUM BIOTECHNOLOGIES, INC.

By: /s/ Leone Patterson
Leone Patterson
Chief Executive Officer and Chief Financial Officer
(Principal Executive and Financial Officer)

Power of Attorney

Each person whose individual signature appears below hereby authorizes and appoints Leone Patterson, 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/Leone Patterson Leone Patterson	Chief Executive Officer, Chief Financial Officer and Director *(Principal Executive, Financial and Accounting Officer)*	March 06, 2019
/s/ Paul B. Cleveland Paul B. Cleveland	Chairman of the Board	March 06, 2019
/s/ Mitchell H. Finer Mitchell H. Finer, Ph.D.	Director	March 06, 2019
/s/ Thomas F. Woiwode Thomas F. Woiwode, Ph.D.	Director	March 06, 2019
/s/ Eric G. Carter Eric G. Carter, M.D., Ph.D.	Director	March 06, 2019
/s/ Patrick Machado Patrick Machado	Director	March 06, 2019
/s/ Richard N. Spivey Richard N. Spivey, Pharm. D.	Director	March 06, 2019

Exhibit 10.12

ADVERUM BIOTECHNOLOGIES, INC
2014 EQUITY INCENTIVE AWARD PLAN
AMENDED FEBRUARY 14, 2019

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.

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4e.2baciIppA wLlahsnlbaccynlappagni,dwa llcn,tnuohtaiw imil (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.

Exhibit 10.12

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

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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.

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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:

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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:

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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.

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(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.

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.

(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.

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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.

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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.

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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

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Administrator may require that, by the terms of the Option, a partial exercise must be with respect to a minimum number of Shares.

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ARTICLE 8.

AWARD OF RESTRICTED STOCK

8.1 Award of Restricted Stock.

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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.

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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.

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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.

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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.

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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:

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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

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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.

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(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.

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(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).

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(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.

Shares Subject to Award.

ARTICLE 13.

ADMINISTRATION

Administration of Plan.

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(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.

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.

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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:

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(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.

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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.

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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 10.16

ADVERUM BIOTECHNOLOGIES, INC.
2014 EMPLOYEE STOCK PURCHASE PLAN
AMENDED AND RESTATED ON FEBRUARY 14, 2019

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, 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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1035 O'Brien Drive, Menlo Park, CA 94025

Tel +1-650-272-6269

Exhibit 10.32

AMENDMENT TO
CHANGE IN CONTROL AND SEVERANCE AGREEMENT

This Amendment (the "Amendment") to that certain Change in Control and Severance

Agreement, dated as of November 5, 2014 (the "Severance Agreement"), by and between Mehdi Gasmi, Ph.D. ("Executive") and Avalanche Biotechnologies, Inc. (the "Company") is made as of August 21, 2015 (the "Amendment Effective Date"). Any capitalized term not defined in this Amendment shall have the meaning set forth in the Severance Agreement.

WHEREAS, th e Company desire s to modify the Severance Agreement to motivate Executive to work cooperatively through the leadership transition at the Company.

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NOW, THEREFORE, in consideration of the mutual agreements set forth herein, and for other good and valuable consideration, the receipt of which is hereby acknowledged, the parties hereto hereby agree as follows:

1. Limited Severance Enhancements. If Executive experiences a Covered Termination pursuant to Section 3 of the Severance Agreement prior to the second anniversary of the Amendment Effective Date,

(i) the reference to "nine (9) months" in Section 3(a) of the Severance Agreement shall be replaced with "twelve (12) months" and

(ii) if Executive delivers to the Company a Release of Claims, then in addition to the benefits provided in clauses (a) and (b) of Section 3 of the Severance Agreement, each outstanding equity award, including, without limitation, each stock option and restricted stock unit award, granted prior to August 21, 2015 and 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 that number of shares that would have vested and if, applicable, become exercisable in the twelve (12) months immediately following Executive's Covered Termination had Executive's employment continued during such twelve (12)-month period (the benefits in (i) and (ii), collectively, the "Limited Severance Enhancements"). For the avoidance of doubt, if Executive experiences a Covered Termination pursuant to Section 3 of the Severance Agreement on or after the second anniversary of the Amendment Effective Date, Executive shall not be entitled to the Limited Severance Enhancements.

2. Executive acknowledges and agrees that in connection with the employment of a permanent Chief Scientific Officer of the Company, Executive shall be returned to his position of Senior Vice President, Manufacturing and that the assignment of duties therewith shall not be deemed a material reduction in Executive's duties (as compared to his duties as interim Chief Scientific Officer) for purposes of determining whether Executive has experienced a Constructive Termination pursuant to Sections 3 or 4 of the Severance Agreement.

3. Governing Law. The validity, interpretation, construction and performance of this
Agreement shall be governed by the laws of the State of California.

4. Executive's Successors. The terms of this Amendment 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.

5 . No Other Changes. Except as expressly set forth herein, all of the provisions of the Severance Agreement shall remain unchanged and in full force and effect. After the date hereof, any reference to the Severance Agreement shall mean the Severance Agreement as amended or modified hereby.

6. Counterparts. This Amendment 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.

[*Signature page follows.*]

IN WITNESS WHEREOF, the parties hereto have signed their names as of the day and year first above written.

AVALANCHE BIOTECHNOLOGIES, INC.

By: /s/ Hans Hull
Name: Hans P. Hull
Title: Chief Executive Officer and President

MEHDI GASMI, PH.D.
/s/ Mehdi Gasmi

Exhibit 10.34

ADVERUM BIOTECHNOLOGIES, INC.

2017 INDUCEMENT PLAN

ADOPTED BY THE BOARD OF DIRECTORS: OCTOBER 6, 2017
AMENDED FEBRUARY 14, 2019

1. GENERAL.

(a) **Eligible Award Recipients.** The only persons eligible to receive grants of Awards under this Plan are individuals who satisfy the standards for inducement grants under NASDAQ Marketplace Rule 5635(c)(4) or 5635(c)(3), if applicable, and the related guidance under NASDAQ IM 5635-1. A person who previously served as an Employee or Director will not be eligible to receive Awards under the Plan, other than following a *bona fide* period of non-employment. Persons eligible to receive grants of Awards under this Plan are referred to in this Plan as "***Eligible Employees***." These Awards must be approved by either a majority of the Company's "***Independent Directors***" (as such term is defined in NASDAQ Marketplace Rule 5605(a)(2)) or the Company's compensation committee, provided such committee comprises solely Independent Directors (the "***Independent Compensation Committee***") in order to comply with the exemption from the stockholder approval requirement for "inducement grants" provided under Rule 5635(c)(4) of the NASDAQ Marketplace Rules. NASDAQ Marketplace Rule 5635(c)(4) and the related guidance under NASDAQ IM 5635-1 (and any analogous rules or guidance effective after the date hereof) are referred to in this Plan as the "***Inducement Award Rules***."

(b) **AVAILABLE AWARDS.** The Plan provides for the grant of Options and Restricted Stock Unit Awards. All Options shall be Nonstatutory Stock Options. Awards intended to qualify as stockholder-approved performance based compensation for purposes of Section 162(m) of the Code may not be granted under this Plan.

(c) **Purpose.** This Plan, through the granting of Awards, is intended to provide (i) an inducement material for certain individuals to enter into employment with the Company within the meaning of Rule 5635(c)(4) of the NASDAQ Marketplace Rules, (ii) incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate and (iii) a means by which Eligible Employees may be given an opportunity to benefit from increases in value of the Common Stock through the granting of Awards.

2. ADMINISTRATION.

(a) **ADMINISTRATION BY BOARD.** The Board will administer the Plan; provided, however, that Awards may only be granted by either (i) a majority of the Company's Independent Directors or (ii) the Independent Compensation Committee. Subject to those constraints and the other constraints of the Inducement Award Rules, the Board may delegate some of its powers of administration of the Plan to a Committee, as provided in Section 2(c).

(b) **Powers of Board.** The Board will have the power, subject to, and within the limitations of, the express provisions of the Plan and the Inducement Award Rules:

(i) To determine: (A) who will be granted Awards; (B) when and how each Award will be granted; (C) what type of Award will be granted; (D) the provisions of each Award (which need not be identical), including when a person will be permitted to exercise or otherwise receive cash or Common Stock under the Award; (E) the number of shares of Common Stock subject to, or the cash value of, an Award; and (F) the Fair Market Value applicable to a n Award; provided, however, that Awards may only be granted by either (i) a majority of the Company's Independent Directors or (ii) the Independent Compensation Committee.

(ii) To construe and interpret the Plan and Awards granted under it, and to establish, amend and revoke rules and regulations for administration of the Plan and Awards. The Board, in the exercise of these powers, may correct any defect, omission or inconsistency in the Plan or in any Award Agreement, in a manner and to the extent it will deem necessary or expedient to make the Plan or Award fully effective.

(iii) To settle all controversies regarding the Plan and Awards granted under it.

(iv) To accelerate, in whole or in part, the time at which an Award may be exercised or vest (or at which cash or shares of Common Stock may be issued).

(v) To suspend or terminate the Plan at any time. Except as otherwise provided in the Plan or an Award Agreement, suspension or termination of the Plan will not materially impair a Participant's rights under his or her then-outstanding Award without his or her written consent.

(vi) To amend the Plan in any respect the Board deems necessary or advisable, including, without limitation, by adopting amendments relating to nonqualified deferred compensation under Section 409A of the Code and/or to bring the Plan or Awards granted under the Plan into compliance therewith, subject to the limitations, if any, of applicable law. Except as provided in Section 9(a) relating to Capitalization Adjustments, if required by applicable law or listing requirements, the Company shall seek stockholder approval for any amendment of the Plan. Except as provided above, rights under any Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (1) the Company requests the consent of the affected Participant, and (2) such Participant consents in writing.

(vii) To submit any amendment to the Plan for stockholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Rule 16b-3 of Exchange Act or any successor rule.

(viii) To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more outstanding Awards. Except as otherwise provided in the Plan or an Award Agreement, no amendment of an outstanding Award will materially impair that Participant's rights under his or her outstanding Award without his or her written consent. To be clear, unless prohibited by applicable law, the Board may amend the terms of an Award without the affected Participant's consent if necessary (A) to clarify the manner of exemption from, or to bring the Award into compliance with, Section 409A of the Code, or (C) to comply with other applicable laws or listing requirements.

(ix) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and that are not in conflict with the provisions of the Plan or Awards.

(x) To adopt such procedures and sub-plans as are necessary or appropriate to permit participation in the Plan by individuals who are foreign nationals or employed outside the United States.

(c) **Delegation to Committee.** The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee will have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board will thereafter be to the Committee or subcommittee). Any delegation of administrative powers will be reflected in resolutions, not inconsistent with the provisions of the Plan, adopted from time to time by the Board or Committee (as applicable). The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated.

(d) **Effect of Board's Decision.** All determinations, interpretations and constructions made by the Board in good faith will not be subject to review by any person and will be final, binding and conclusive on all persons.

(e) **Repricing; Cancellation and Re-Grant of Awards.** Neither the Board nor any Committee will have the authority to: (i) reduce the exercise, purchase or strike price of any outstanding Option, or (ii) cancel any outstanding Option that has an exercise price or strike price greater than the current Fair Market Value of the Common Stock in exchange for cash or other Awards under the Plan, unless the stockholders of the Company have approved such an action within twelve (12) months prior to such an event.

3. Shares Subject to the Plan.

(a) **Share Reserve.** Subject to Section 9(a) relating to Capitalization Adjustments, the aggregate number of shares of Common Stock that may be issued pursuant to Awards from and after the Effective Date shall not exceed 1,500,000 shares. Shares may be issued under the terms of this Plan in connection with a merger or acquisition as permitted by NASDAQ Marketplace Rule 5635(c)(3), NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable rule, and such issuance will not reduce the number of shares available for issuance under the Plan.

(b) **Reversion of Shares to the Share Reserve.** If an Award or any portion thereof (i) expires or otherwise terminates without all of the shares covered by such Award having been issued or (ii) is settled in cash (*i.e.*, the Participant receives cash rather than stock), such expiration, termination or settlement will not reduce (or otherwise offset) the number of shares of Common Stock that may be available for issuance under the Plan. If any shares of Common Stock issued pursuant to an Award are forfeited back to or repurchased by the Company because of the failure

to meet a contingency or condition required to vest such shares in the Participant, then the shares that are forfeited or repurchased will revert to and again become available for issuance under the Plan. Any shares reacquired by the Company in satisfaction of tax withholding obligations on an Award or as consideration for the exercise or purchase price of an Award will again become available for issuance under the Plan.

(c) **Source of Shares.** The stock issuable under the Plan will be shares of authorized but unissued or reacquired Common Stock, including shares repurchased by the Company on the open market or otherwise.

4. Eligibility.

(a) **Eligibility for Awards.** Awards may only be granted to persons who are Eligible Employees described in Section 1(a) of the Plan, where the Award is an inducement material to the individual's entering into employment with the Company or an Affiliate within the meaning of Rule 5635(c)(4) of the NASDAQ Marketplace Rules or is otherwise permitted pursuant to Rule 5635(c) of the NASDAQ Marketplace Rules, *provided however*, that Awards may not be granted to Eligible Employees who are providing Continuous Service only to any "parent" of the Company, as such term is defined in Rule 405 of the Securities Act, unless (i) the stock underlying such Awards is treated as "service recipient stock" under Section 409A of the Code (for example, because the Awards are granted pursuant to a corporate transaction such as a spin off transaction), or (ii) the Company, in consultation with its legal counsel, has determined that such Awards are otherwise exempt from or comply with the distribution requirements of Section 409A of the Code.

(b) **Approval Requirements.** All Awards must be granted either by a majority of the Company's independent directors or the Independent Compensation Committee.

5. Provisions relating to Options.

Each Option will be in such form and will contain such terms and conditions as the Board deems appropriate. All Options will be Nonstatutory Stock Options. The provisions of separate Options need not be identical; *provided, however*, that each Option Agreement will conform to (through incorporation of provisions hereof by reference in the applicable Option Agreement or otherwise) the substance of each of the following provisions:

(a) **Term.** No Option will be exercisable after the expiration of 10 years from the date of its grant or such shorter period specified in the Option Agreement.

(b) **Exercise Price.** The exercise or strike price of each Option will be not less than 100% of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Option may be granted with an exercise price lower than 100% of the Fair Market Value of the Common Stock subject to the Option if such Option is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Section 409A of the Code.

(c) **Purchase Price for Options.** The purchase price of Common Stock acquired pursuant to the exercise of an Option may be paid, to the extent permitted by applicable law and

as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board will have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to use a particular method of payment. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of the stock subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of shares of Common Stock;

(iv) by a "net exercise" arrangement pursuant to which the Company will reduce the number of shares of Common Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that the Company will accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole shares to be issued. Shares of Common Stock will no longer be subject to an Option and will not be exercisable thereafter to the extent that (A) shares issuable upon exercise are reduced to pay the exercise price pursuant to the "net exercise," (B) shares are delivered to the Participant as a result of such exercise, and (C) shares are withheld to satisfy tax withholding obligations; or

(v) in any other form of legal consideration that may be acceptable to the Board and specified in the applicable Award Agreement.

(d) Transferability of Options. The Board may, in its sole discretion, impose such limitations on the transferability of Options as the Board will determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options will apply:

(i) Restrictions on Transfer. An Option will not be transferable except by will or by the laws of descent and distribution (or pursuant to subsections (ii) and (iii) below), and will be exercisable during the lifetime of the Participant only by the Participant. The Board may permit transfer of the Option in a manner that is not prohibited by applicable tax and securities laws. Except as explicitly provided herein, an Option may not be transferred for consideration.

(ii) Domestic Relations Orders. Subject to the approval of the Board or a duly authorized Officer, an Option may be transferred pursuant to the terms of a domestic relations order or official marital settlement agreement or other divorce or separation instrument.

(iii) Beneficiary Designation. Subject to the approval of the Board or a duly authorized Officer, a Participant may, by delivering written notice to the Company, in a form approved by the Company (or the designated broker), designate a third party who, on the death of

the Participant, will thereafter be entitled to exercise the Option and receive the Common Stock or other consideration resulting from such exercise. In the absence of such a designation, the executor or administrator of the Participant's estate will be entitled to exercise the Option and receive the Common Stock or other consideration resulting from such exercise. However, the Company may prohibit designation of a beneficiary at any time, including due to any conclusion by the Company that such designation would be inconsistent with the provisions of applicable laws.

(e) **Vesting Generally.** The total number of shares of Common Stock subject to an Option may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of Performance Goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary. The provisions of this Section are subject to any Option provisions governing the minimum number of shares of Common Stock as to which an Option may be exercised.

(f) **Termination of Continuous Service.** Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company, if a Participant's Continuous Service terminates (other than for Cause and other than upon the Participant's death or Disability), the Participant may exercise his or her Option (to the extent that the Participant was entitled to exercise such Award as of the date of termination of Continuous Service) within the period of time ending on the earlier of (i) the date three months following the termination of the Participant's Continuous Service and (ii) the expiration of the term of the Option as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option within the applicable time frame, the Option will terminate.

(g) **Extension of Termination Date.** If the exercise of an Option following the termination of the Participant's Continuous Service (other than for Cause and other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option will terminate on the earlier of (i) the expiration of a total period of three months (that need not be consecutive) after the termination of the Participant's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements, and (ii) the expiration of the term of the Option as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the sale of any Common Stock received on exercise of an Option following the termination of the Participant's Continuous Service (other than for Cause) would violate the Company's insider trading policy, then the Option will terminate on the earlier of (i) the expiration of a period of months (that need not be consecutive) equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of the Common Stock received upon exercise of the Option would not be in violation of the Company's insider trading policy, or (ii) the expiration of the term of the Option as set forth in the applicable Award Agreement.

(h) **Disability of Participant.** Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company, if a Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Option (to the extent that the Participant was entitled to exercise such Option as of the date of termination of Continuous Service), but only within such period of time ending

on the earlier of (i) the date 12 months following such termination of Continuous Service and (ii) the expiration of the term of the Option as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option within the applicable time frame, the Option (as applicable) will terminate.

(i) **Death of Participant.** Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company, if (i) a Participant's Continuous Service terminates as a result of the Participant's death, or (ii) the Participant dies within the period (if any) specified in the Award Agreement for exercisability after the termination of the Participant's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Participant was entitled to exercise such Option as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated to exercise the Option upon the Participant's death, but only within the period ending on the earlier of (i) the date 18 months following the date of death and (ii) the expiration of the term of such Option as set forth in the Award Agreement. If, after the Participant's death, the Option is not exercised within the applicable time frame, the Option will terminate.

(j) **Termination for Cause.** Except as explicitly provided otherwise in a Participant's Award Agreement, if a Participant's Continuous Service is terminated for Cause, the Option will terminate upon the date on which the event giving rise to the termination for Cause first occurred, and the Participant will be prohibited from exercising his or her Option from and after the date on which the event giving rise to the termination for Cause first occurred (or, if required by law, the date of termination of Continuous Service).

(k) **Non-Exempt Employees.** If an Option is granted to an Employee who is a non-exempt employee for purposes of the Fair Labor Standards Act of 1938, as amended, the Option will not be first exercisable for any shares of Common Stock until at least six (6) months following the date of grant of the Option (although the Award may vest prior to such date). Consistent with the provisions of the Worker Economic Opportunity Act, (i) if such non-exempt Employee dies or suffers a Disability, (ii) upon a Corporate Transaction in which such Option is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement in another agreement between the Participant and the Company, or, if no such definition, in accordance with the Company's then current employment policies and guidelines), the vested portion of any Options may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option will be exempt from his or her regular rate of pay. To the extent permitted and/or required for compliance with the Worker Economic Opportunity Act to ensure that any income derived by a non-exempt employee in connection with the exercise, vesting or issuance of any shares under any other Award will be exempt from the employee's regular rate of pay, the provisions of this Section will apply to all Awards and are hereby incorporated by reference into such Award Agreements.

6. Provisions Relating to Restricted Stock Unit Awards.

Each Restricted Stock Unit Award Agreement will be in such form and will contain such terms and conditions as the Board will deem appropriate. The terms and conditions of Restricted Stock Unit Award Agreements may change from time to time, and the terms and conditions of separate Restricted Stock Unit Award Agreements need not be identical. Each Restricted Stock Unit Award Agreement will conform to (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(a) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Common Stock subject to the Restricted Stock Unit Award. The consideration to be paid (if any) by the Participant for each share of Common Stock subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

(b) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(c) Payment. A Restricted Stock Unit Award may be settled by the delivery of shares of Common Stock, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement.

(d) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the shares of Common Stock (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(e) Dividend Equivalents. Dividend equivalents may be credited in respect of shares of Common Stock covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional shares of Common Stock covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any additional shares covered by the Restricted Stock Unit Award credited by reason of such dividend equivalents will be subject to all of the same terms and conditions of the underlying Restricted Stock Unit Award Agreement to which they relate.

(f) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Restricted Stock Unit Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

7. Covenants of the Company.

(a) Availability of Shares. The Company will keep available at all times the number of shares of Common Stock reasonably required to satisfy then-outstanding Awards.

(b) **Securities Law Compliance.** The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Awards and to issue and sell shares of Common Stock upon exercise of the Awards; *provided, however*, that this undertaking will not require the Company to register under the Securities Act the Plan, any Award or any Common Stock issued or issuable pursuant to any such Award. If, after reasonable efforts and at a reasonable cost, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company will be relieved from any liability for failure to issue and sell Common Stock upon exercise of such Awards unless and until such authority is obtained. A Participant will not be eligible for the grant of an Award or the subsequent issuance of cash or Common Stock pursuant to the Award if such grant or issuance would be in violation of any applicable securities law.

(c) **No Obligation to Notify or Minimize Taxes.** The Company will have no duty or obligation to any Participant to advise such holder as to the time or manner of exercising such Award. Furthermore, the Company will have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of an Award or a possible period in which the Award may not be exercised. The Company has no duty or obligation to minimize the tax consequences of an Award to the holder of such Award.

8. **Miscellaneous.**

(a) **Use of Proceeds from Sales of Common Stock.** Proceeds from the sale of shares of Common Stock pursuant to Awards will constitute general funds of the Company.

(b) **Corporate Action Constituting Grant of Awards.** Corporate action constituting a grant by the Company of an Award to any Participant will be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Award is communicated to, or actually received or accepted by, the Participant. In the event that the corporate records (e.g., Board consents, resolutions or minutes) documenting the corporate action constituting the grant contain terms (e.g., exercise price, vesting schedule or number of shares) that are inconsistent with those in the Award Agreement as a result of a clerical error in the papering of the Award Agreement, the corporate records will control and the Participant will have no legally binding right to the incorrect term in the Award Agreement.

(c) **Stockholder Rights.** No Participant will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to an Award unless and until (i) such Participant has satisfied all requirements for exercise of, or the issuance of shares under, the Award pursuant to its terms, and (ii) the issuance of the Common Stock subject to such Award has been entered into the books and records of the Company.

(d) **No Employment or Other Service Rights.** Nothing in the Plan, any Award Agreement or any other instrument executed thereunder or in connection with any Award granted pursuant thereto will confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Award was granted or will affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice

and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate, or (iii) the service of a Director pursuant to the bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(e) **CHANGE IN TIME COMMITMENT.** In the event a Participant's regular level of time commitment in the performance of his or her services for the Company and any Affiliates is reduced (for example, and without limitation, if the Participant is an Employee of the Company and the Employee has a change in status from a full-time Employee to a part-time Employee) after the date of grant of any Award to the Participant, the Board has the right in its sole discretion to (x) make a corresponding reduction in the number of shares or cash amount subject to any portion of such Award that is scheduled to vest or become payable after the date of such change in time commitment, and (y) in lieu of or in combination with such a reduction, extend the vesting or payment schedule applicable to such Award. In the event of any such reduction, the Participant will have no right with respect to any portion of the Award that is so reduced.

(f) **INVESTMENT ASSURANCES.** The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Common Stock subject to the Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, will be inoperative if (A) the issuance of the shares upon the exercise or acquisition of Common Stock under the Award has been registered under a then currently effective registration statement under the Securities Act, or (B) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(g) **Withholding Obligations.** Unless prohibited by the terms of an Award Agreement, the Company may, in its sole discretion, satisfy any federal, state or local tax withholding obligation relating to an Award by any of the following means or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding shares of Common Stock from the shares of Common Stock issued or otherwise issuable to the Participant in connection with the Award; *provided, however,* that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such lesser amount as may be necessary to avoid classification of the Award as a liability for financial accounting purposes); (iii) withholding cash from an Award settled in cash; (iv) withholding payment from any amounts otherwise payable to the Participant; or (v) by such other method as may be set forth in the Award Agreement.

(h) **Electronic Delivery** Any reference herein to a "written" agreement or document will include any agreement or document delivered electronically, filed publicly at www.sec.gov (or any successor website thereto) or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

(i) **Deferrals.** To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Common Stock or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee or otherwise providing services to the Company. The Board is authorized to make deferrals of Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of Continuous Service, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(j) **Compliance with Section 409A.** Unless otherwise expressly provided for in an Award Agreement, the Plan and Award Agreements will be interpreted to the greatest extent possible in a manner that makes the Plan and the Awards granted hereunder exempt from Section 409A of the Code, and, to the extent not so exempt, in compliance with Section 409A of the Code. If the Board determines that any Award granted hereunder is not exempt from and is therefore subject to Section 409A of the Code, the Award Agreement evidencing such Award will incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code, and to the extent an Award Agreement is silent on terms necessary for compliance, such terms are hereby incorporated by reference into the Award Agreement. Notwithstanding anything to the contrary in this Plan (and unless the Award Agreement specifically provides otherwise), if the shares of Common Stock are publicly traded, and if a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount that is due because of a "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) will be issued or paid before the date that is six (6) months following the date of such Participant's "separation from service" or, if earlier, the date of the Participant's death, unless such distribution or payment can be made in a manner that complies with Section 409A of the Code, and any amounts so deferred will be paid in a lump sum on the day after such six (6) month period elapses, with the balance paid thereafter on the original schedule.

(k) **Clawback/Recovery.** All Awards granted under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board may impose such other clawback, recovery or recoupment provisions in an Award Agreement as the Board determines necessary or appropriate, including but not limited to a reacquisition right in respect of previously acquired shares of Common Stock or other cash or property upon the occurrence of Cause.

9. Adjustments upon Changes in Common Stock; Other Corporate Events.

(a) **Capitalization Adjustments.** In the event of a Capitalization Adjustment, the Board will appropriately and proportionately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a); and (ii) the class(es) and number of securities and price per share of stock subject to outstanding Awards. The Board will make such adjustments, and its determination will be final, binding and conclusive.

(b) **Dissolution or Liquidation.** Except as otherwise provided in the Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Awards (other than Awards consisting of vested and outstanding shares of Common Stock not subject to a forfeiture condition or the Company's right of repurchase) will terminate immediately prior to the completion of such dissolution or liquidation, and the shares of Common Stock subject to the Company's repurchase rights or subject to a forfeiture condition may be repurchased or reacquired by the Company notwithstanding the fact that the holder of such Award is providing Continuous Service; *provided, however*, that the Board may, in its sole discretion, cause some or all Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c) **Corporate Transaction.** The following provisions will apply to Awards in the event of a Corporate Transaction unless otherwise provided in the instrument evidencing the Award or any other written agreement between the Company or any Affiliate and the Participant or unless otherwise expressly provided by the Board at the time of grant of an Award. In the event of a Corporate Transaction, then, notwithstanding any other provision of the Plan, the Board will take one or more of the following actions with respect to Awards, contingent upon the closing or completion of the Corporate Transaction:

(i) arrange for the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) to assume or continue the Award or to substitute a similar award for the Award (including, but not limited to, an award to acquire the same consideration paid to the stockholders of the Company pursuant to the Corporate Transaction);

(ii) arrange for the assignment of any reacquisition or repurchase rights held by the Company in respect of Common Stock issued pursuant to the Award to the surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company);

(iii) accelerate the vesting, in whole or in part, of the Award (and, if applicable, the time at which the Award may be exercised) to a date prior to the effective time of such Corporate Transaction as the Board will determine (or, if the Board will not determine such a date, to the date that is five days prior to the effective date of the Corporate Transaction), with such Award terminating if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction;

(iv) arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by the Company with respect to the Award;

(v) cancel or arrange for the cancellation of the Award, to the extent not vested or not exercised prior to the effective time of the Corporate Transaction, in exchange for such cash consideration, if any, as the Board, in its sole discretion, may consider appropriate; and

(vi) make a payment, in such form as may be determined by the Board equal to the excess, if any, of (A) the value of the property the Participant would have received upon the exercise of the Award immediately prior to the effective time of the Corporate Transaction, over (B) any exercise price payable by such holder in connection with such exercise. For clarity, this payment may be zero ($) if the value of the property is equal to or less than the exercise price. Payments under this provision may be delayed to the same extent that payment of consideration to the holders of the Company's Common Stock in connection with the Corporate Transaction is delayed as a result of escrows, earn-outs, holdbacks or any other contingencies.

The Board need not take the same action or actions with respect to all Awards or portions thereof or with respect to all Participants.

(d) **Change in Control.** In the event of a Change in Control, the Board shall have the discretion to take any one or more of the actions set forth in Section 9(c)(i)-(vi) with respect to Awards, contingent upon the closing or completion of the Change in Control; *provided, however*, that for such purpose, the term "Corporate Transaction" in Section 9(c)(i)-(vi) will mean "Change In Control." An Award may be subject to additional acceleration of vesting and exercisability upon or after a Change in Control as may be provided in the Award Agreement for such Award or as may be provided in any other written agreement between the Company or any Affiliate and the Participant.

10. Termination or Suspension of the Plan.

The Board may suspend or terminate the Plan at any time. No Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

11. Effective Date of the Plan.

The Plan will come into existence on the Effective Date. No Award may be granted prior to the Effective Date.

12. Choice of Law.

The law of the State of Delaware will govern all questions concerning the construction, validity and interpretation of this Plan, without regard to that state's conflict of laws rules.

13. Definitions. As used in the Plan, the following definitions will apply to the capitalized terms indicated below:

(a) "***Affiliate***" means, at the time of determination, any "parent" or "subsidiary" of the Company as such terms are defined in Rule 405 of the Securities Act. The Board will have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition.

(b) "***Award***" means a Nonstatutory Stock Option or a Restricted Stock Unit Award.

(c) "***Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of an Award.

(d) "***Board***" means the Board of Directors of the Company.

(e) "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Common Stock subject to the Plan or subject to any Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or any similar equity restructuring transaction, as that term is used in Statement of Financial Accounting Standards Board Accounting Standards Codification Topic 718 (or any successor thereto). Notwithstanding the foregoing, the conversion of any convertible securities of the Company shall not be treated as a Capitalization Adjustment.

(f) "***Cause***" shall have the meaning ascribed to such term in any written agreement between the Participant and the Company defining such term (and if there are multiple such agreements, the most recent) and, in the absence of such agreement, such term means, with respect to a Participant, the occurrence of any of the following events: [(i) the Participant's commission of any crime involving fraud, dishonesty or moral turpitude; (ii) the Participant's attempted commission of or participation in a fraud or act of dishonesty against the Company that results in (or might have reasonably resulted in) material harm to the business of the Company; (iii) the Participant's intentional, material violation of any contract or agreement between the Participant and the Company or any statutory duty that the Participant owes to the Company; or (iv) the Participant's conduct that constitutes gross insubordination, incompetence or habitual neglect of duties and that results in (or might have reasonably resulted in) material harm to the business of the Company; *provided, however*, that the action or conduct described in clauses (iii) and (iv) above will constitute "***Cause***" only if such action or conduct continues after the Company has provided the Participant with written notice thereof and thirty (30) days to cure the same][1].

(g) "***Change in Control***" means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction. Notwithstanding the foregoing, a Change in Control will not be deemed to occur (A) on account of the acquisition of securities of the Company directly from the Company; (B) on account of the acquisition of securities of the Company by an investor, any affiliate thereof or any other Exchange Act Person that acquires the Company's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Company through the issuance of equity securities; or (C) solely because the level of Ownership held by any Exchange Act Person (the "***Subject Person***") exceeds the designated percentage threshold of the

[1] If the Company has a preferred/standard definition of Cause, it could be inserted here instead.

outstanding voting securities as a result of a repurchase or other acquisition of voting securities by the Company reducing the number of shares outstanding, provided that if a Change in Control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by the Company, and after such share acquisition, the Subject Person becomes the Owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting securities Owned by the Subject Person over the designated percentage threshold, then a Change in Control will be deemed to occur;

(ii) there is consummated a merger, consolidation or similar transaction involving (directly or indirectly) the Company and, immediately after the consummation of such merger, consolidation or similar transaction, the stockholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing more than 50% of the combined outstanding voting power of the surviving Entity in such merger, consolidation or similar transaction or (B) more than 50% of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction, in each case in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such transaction;

(iii) there is consummated a sale, lease, exclusive license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than fifty percent (50%) of the combined voting power of the voting securities of which are Owned by stockholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, license or other disposition; or

(iv) individuals who, on the date the Plan is adopted by the Board, are members of the Board (the "***Incumbent Board***") cease for any reason to constitute at least a majority of the members of the Board; *provided, however*, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member will, for purposes of this Plan, be considered as a member of the Incumbent Board.

For purposes of determining voting power under the term Change in Control, voting power shall be calculated by assuming the conversion of all equity securities convertible (immediately or at some future time) into shares entitled to vote, but not assuming the exercise of any warrant or right to subscribe to or purchase those shares. In addition, (A) the term Change in Control will not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, (B) the term Change in Control will not include a change in the voting power of any one or more stockholders as a result of the conversion of any class of the Company's securities into another class of the Company's securities having a different number of votes per share pursuant to the conversion provisions set forth in the Company's Amended and Restated Certificate of Incorporation, and (C) the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant will supersede the foregoing definition with respect to Awards subject to such agreement; *provided, however*, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition will apply. If required

for compliance with Section 409A of the Code, in no event will a Change in Control be deemed to have occurred if such transaction is not also a "change in the ownership or effective control of" the Company or "a change in the ownership of a substantial portion of the assets of" the Company as determined under Treasury Regulation Section 1.409A-3(i)(5) (without regard to any alternative definition thereunder). The Board may, in its sole discretion and without a Participant's consent, amend the definition of "Change in Control" to conform to the definition of "Change in Control" under Section 409A of the Code, and the regulations thereunder.

(h) "***Code***" means the Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

(i) "***Committee***" means a committee of one or more Independent Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

(j) "***Common Stock***" means the common stock of the Company, par value $0.0001 per share, having one vote per share.

(k) "***Company***" means Adverum Biotechnologies, Inc., a Delaware corporation.

(l) "***Consultant***" means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Director, or payment of a fee for such service, will not cause a Director to be considered a "Consultant" for purposes of the Plan. Notwithstanding the foregoing, a person is treated as a Consultant under this Plan only if a Form S-8 Registration Statement under the Securities Act is available to register either the offer or the sale of the Company's securities to such person.

(m) "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, will not terminate a Participant's Continuous Service ; *provided, however*, that if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board, in its sole discretion, such Participant's Continuous Service will be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service will be considered interrupted in the case of (i) any leave of absence approved by the Board or chief executive officer, including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence will be treated as Continuous Service for purposes of vesting in an Award only to such extent as may be provided in the Company's leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law. In addition, to the extent required for exemption from or compliance with Section 409A of the Code, the determination of whether there has been a termination of Continuous Service will be made, and such term will be

construed, in a manner that is consistent with the definition of "separation from service" as defined under Treasury Regulation Section 1.409A-1(h) (without regard to any alternative definition thereunder).

(n) "***Corporate Transaction***" means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) the consummation of a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

(ii) the consummation of a sale or other disposition of at least 50% of the outstanding securities of the Company;

(iii) the consummation of a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

(iv) the consummation of a merger, consolidation or similar transaction following which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

To the extent required for compliance with Section 409A of the Code, in no event will an event be deemed a Corporate Transaction if such transaction is not also a "change in the ownership or effective control of" the Company or "a change in the ownership of a substantial portion of the assets of" the Company as determined under Treasury Regulation Section 1.409A-3(i)(5) (without regard to any alternative definition thereunder).

(o) "***Director***" means a member of the Board. Directors are not eligible to receive Awards under the Plan with respect to their service in such capacity.

(p) "***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or that has lasted or can be expected to last for a continuous period of not less than 12 months, as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and will be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(q) "***Effective Date***" means _____, 2017.

(r) "***Employee***" means any person employed by the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such services, will not cause a Director to be considered an "Employee" for purposes of the Plan.

(s) "***Entity***" means a corporation, partnership, limited liability company or other entity.

(t) "***Exchange Act***" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

(u) "***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" will not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, (iv) an Entity Owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their Ownership of stock of the Company; or (v) any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the Effective Date, is the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities.

(v) "***Fair Market Value***" means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on any established market, the Fair Market Value of a share of Common Stock will be, unless otherwise determined by the Board, the closing sales price for such stock as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the date of determination, as reported in a source the Board deems reliable.

(ii) Unless otherwise provided by the Board, if there is no closing sales price for the Common Stock on the date of determination, then the Fair Market Value will be the closing selling price on the last preceding date for which such quotation exists.

(iii) In the absence of such markets for the Common Stock, the Fair Market Value will be determined by the Board in good faith and in a manner that complies with Sections 409A and 422 of the Code.

(w) "***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("***Regulation S-K***")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

(x) "***Nonstatutory Stock Option***" means any option granted pursuant to Section 5 of the Plan that does not qualify as an "incentive stock option" within the meaning of Section 422 of the Code.

(y) "***Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

(z) "***Option***" means a Nonstatutory Stock Option to purchase shares of Common Stock granted pursuant to the Plan.

(aa) "***Option Agreement***" means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an Option grant. Each Option Agreement will be subject to the terms and conditions of the Plan.

(bb) "***Optionholder***" means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(cc) "***Own,***" "***Owned,***" "***Owner,***" "***Ownership***" **A** person or Entity will be deemed to "Own," to have "Owned," to be the "Owner" of, or to have acquired "Ownership" of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(dd) "***Participant***" means a person to whom an Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Award.

(ee) "***Plan***" means this Adverum Biotechnologies, Inc. 2017 Inducement Plan, as it may be amended.

(ff) "***Restricted Stock Unit Award***" means a right to receive shares of Common Stock which is granted pursuant to the terms and conditions of Section 6.

(gg) "***Restricted Stock Unit Award Agreement***" means a written agreement between the Company and a holder of a Restricted Stock Unit Award evidencing the terms and conditions of a Restricted Stock Unit Award grant. Each Restricted Stock Unit Award Agreement will be subject to the terms and conditions of the Plan.

(hh) "***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(ii) "***Securities Act***" means the Securities Act of 1933, as amended.

(jj) "***Subsidiary***" means, with respect to the Company, (i) any corporation of which more than 50% of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation will have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than 50%.

[*] = 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 10.46

UNIVERSITY OF CALIFORNIA, BERKELEY
OFFICE OF TECHNOLOGY LICENSING

EXCLUSIVE LICENSE AND BAILMENT AGREEMENT

BETWEEN

AVALANCHE BIOTECHNOLOGIES, INC.

AND

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

FOR

[*]

UC Case Nos.: [*]

EXCLUSIVE LICENSE and BAILMENT AGREEMENT
FOR
[*]

UC Case Nos.: [*]

This exclusive license agreement ("Agreement") is effective June 17, 2013 ("Effective Date"), by and between THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, a California corporation, whose legal address is 1111 Franklin Street, 12th Floor, Oakland, California 94607- 5200, acting through its Office of Technology Licensing, at the University of California, Berkeley, 2150 Shattuck Avenue, Suite 510, Berkeley, CA 94704-1347 ("REGENTS") and AVALANCHE BIOTECHNOLOGIES, INC., a Delaware corporation having a principal place of business at 665 Third Street, Suite 250, San Francisco, CA 94107 ("LICENSEE"). The parties agree as follows:

1. BACKGROUND

1.1 REGENTS has assignments to the following (collectively referred to as "INVENTIONS"): invention disclosures entitled, [*] invented by [*] employed by the University of California, Berkeley, as described in REGENTS' case No.: [*]; and [*] invented by [*] employed by the University of California, Berkeley, as described in REGENTS' case No.: [*] and to REGENTS' PATENT RIGHTS, as hereinafter defined, which are directed to the INVENTIONS.

1.2 LICENSEE entered into an option agreement with REGENTS effective [*], terminating on [*], for the purpose of evaluating the INVENTIONS and granting LICENSEE an exclusive right to negotiate an exclusive license in REGENTS' PATENT RIGHTS to the INVENTIONS, which Option Agreement covers LICENSEE's commitment to reimburse REGENTS' patent costs during the period.

1.3 LICENSEE has provided REGENTS with a commercialization plan for the INVENTIONS and business strategy in order to evaluate its capabilities as a LICENSEE.

1.4 The development of the INVENTIONS was sponsored in part by various grants by U.S. Government agencies, and as a consequence, REGENTS elected to retain title to the INVENTIONS subject to the rights of the U.S. Government under 35 USC 200-212 and implementing regulations, including that REGENTS, in turn, has granted back to the U.S. Government a non-exclusive, non-transferrable irrevocable, paid-up license to practice or have practiced the INVENTIONS for or on behalf of the U.S. Government throughout the world. These U.S. Government grants are [*]

1.5 REGENTS and LICENSEE wish to have the INVENTIONS perfected and marketed as soon as reasonably practicable so that products resulting therefrom may be available for public use and benefit.

1.6 LICENSEE wishes to acquire, and REGENTS wishes to grant to LICENSEE, an exclusive license under REGENTS' PATENT RIGHTS and an exclusive bailment of the BIOLOGICAL MATERIAL under the REGENTS' PROPERTY RIGHTS for the purpose of undertaking development and to make, have made, use, sell, offer for sale, import, and export LICENSED PRODUCTS as defined below.

2. DEFINITIONS

2.1 "REGENTS' PATENT RIGHTS" means REGENTS' rights in the following U.S. and foreign patent applications:

i. [*] Patent Application Number [*], entitled "[*]" (UC Case No. [*]), filed on [*] and assigned to REGENTS;

ii. [*] Patent Application Number [*], entitled "[*]" (UC Case No. [*]), filed on [*] and assigned to REGENTS;

iii. [*] Patent Application Number [*] entitled [*] filed on [*] and assigned to REGENTS;

iv. [*] Patent Application Number [*] entitled [*] filed on [*] and assigned to REGENTS, and

v. All other international patents and patent applications, and/or any divisions, continuations, reissues or continuations-in-part (only to the extent, however, that claims in the continuations-in-part are entitled to the priority filing date of the parent patent application) of any of the above-referenced U.S. or international patents or applications.

2.2 "LICENSED PRODUCTS" means all kits, compositions of matter, articles of manufacture, materials, and products, the manufacture, use, SALE, offer for SALE, or import of which: a) requires the performance of the LICENSED METHOD; or b) but for the license granted pursuant to this Agreement, would infringe, or contribute to or induce the infringement of, a VALID CLAIM under REGENTS' PATENT RIGHTS.

2.3 "LICENSED METHOD" means any process or method the use or practice of which, but for the license pursuant to this Agreement, would infringe, or contribute to or induce the infringement of a VALID CLAIM under REGENTS' PATENT RIGHTS in that country in which the LICENSED METHOD is used or practiced.

2.4 "LICENSED FIELD OF USE" means [*]

2.5 "NET SALES" means the gross invoice price charged, and the value of non-cash consideration owed to, LICENSEE or a sublicensee for SALES of LICENSED PRODUCTS, LICENSED SERVICES, and LICENSED METHODS in the LICENSED TERRITORY, the less the sum of the following actual and customary deductions where applicable: cash, trade or quantity discounts; sales, use, tariff, import/export duties or other excise taxes when included in gross sales, Deductable Value-Added Tax, but excluding value-added taxes other than Deductable Value Added Tax or taxes assessed on income derived from sales: "Deductable Value-Added Tax" means value-added tax only to the extent that such value-added tax is actually incurred and is not reimbursable, refundable, or creditable under the tax authority of any country; freight, insurance, packaging costs, and transportation

charges; allowances or credits to customers because of rejections or returns, because of retroactive price reductions, or due to recalls; provisions for actual uncollectible accounts determined in accordance with US GAAP; and discounts, rebates or similar payments granted or given to wholesalers or other distributors, buying groups, health care insurance carriers or other institutions or to the government, including Medicare/Medicaid and other government rebates/discounts. For purposes of calculating NET SALES, a SALE to a sublicensee for end use by the sublicensee will be treated as a SALE at wholesale price. NET SALES shall exclude any disposition of LICENSED PRODUCTS, LICENSED SERVICES and LICENSED METHODS in connection with clinical trials thereof and any disposition of LICENSED PRODUCTS distributed for promotional or charitable purposes, in reasonable quantities.

2.6 "AFFILIATE" of LICENSEE means any entity that, directly or indirectly, Controls LICENSEE, is Controlled by LICENSEE, or is under common Control with LICENSEE. "Control" means (i) having the actual, present capacity to elect a majority of the directors of such affiliate, or (ii) having the power to direct at least [*] of the voting rights entitled to elect directors, or (iii) in any country where the local law will not permit foreign equity participation of a majority, ownership or control, directly or indirectly, of the maximum percentage of such outstanding stock or voting rights permitted by local law.

2.7 "LICENSED TERRITORY" means [*]

2.8 "SALE" means, for LICENSED PRODUCTS and LICENSED SERVICES, the act of selling, leasing or otherwise transferring, providing, or furnishing such product or service, and for LICENSED METHOD the act of performing such method, for any use or for any consideration. Correspondingly, "SELL" means to make or cause to be made a SALE, and "SOLD" means to have made or caused to be made a SALE.

2.9 "LICENSED SERVICE" means a service provided using LICENSED PRODUCTS or LICENSED METHOD.

2.10 "SUBLICENSEE REVENUE" means any cash consideration, and of the cash equivalent of all other consideration, due to LICENSEE under each sublicense for the grant of rights under the REGENTS' PATENT RIGHTS, but excluding: (a) any royalty payments on sales of LICENSED PRODUCTS, LICENSED SERVICES and LICENSED METHODS by a sublicensee (which sales shall be included as NET SALES and shall give rise to royalty payments to REGENTS under section 6.1); (b) any amounts paid by a sublicensee as bona fide reimbursement for research and development costs at fair market value for materials and full time equivalents; (c) bona fide loans or any payments in consideration for a grant of equity of the LICENSEE at fair market value; (d) amounts paid for supplies of product or other tangible materials; (e) amounts paid as reimbursement for expenses directly related to the pursuit, maintenance, and/or defense of REGENTS' PATENT RIGHTS; (f) milestone payments by a sublicensee (which shall be give rise to the milestone payments to REGENTS under section 6.4); and (g) withholding taxes and any other amounts by a sublicensee from amounts otherwise payable to LICENSEE under such sublicense agreement other than past due payments.

2.11 "PHASE IIB CLINICAL TRIAL" means a human clinical trial in any country that would satisfy the requirements of 21 CFR 312.21(b) and that is designed to support and immediately precede the initiation of a Phase III Clinical Trial without any further phase II trials by evaluating the dose-dependent effectiveness of a pharmaceutical product for a particular indication or indications in patients with the disease or condition under study and to determine the common side effects and risks associated with the pharmaceutical product.

2.12 "PHASE III CLINICAL TRIAL" means a human clinical trial in any country that would satisfy the requirements of 21 CFR 312.21(c).

2.13 "VALID CLAIM" shall mean a claim in an issued, unexpired patent or in a pending patent application (which claim is pending for no more than [*] within licensed REGENTS' PATENT RIGHTS that (a) has not been cancelled, withdrawn, abandoned or rejected by any administrative agency or other body of competent jurisdiction from which no appeal has or can be taken, (b) has not been revoked, held invalid, or declared unpatentable or unenforceable in a decision of a court or other body of competent jurisdiction that is unappealable or unappealed within the time allowed for appeal, (c) has not been rendered unenforceable through disclaimer or otherwise, and (d) is not lost through an interference proceeding. If a

claim is pending for more than [*] and latter issues in a patent, then as of the patent issue date, the claim again becomes a VALID CLAIM.

2.14 "FIRST COMMERCIAL SALE" shall mean the first SALE of a LICENSED PRODUCT, LICENSED METHOD or LICENSED SERVICE by LICENSEE or its sublicensees following regulatory approval in the applicable country of sale.

2.15 "REGENTS' PROPERTY RIGHTS" means all of REGENTS' personal property rights in the tangible property in INVENTIONS licensed here under. REGENTS' PROPERTY RIGHTS do not include REGENTS' PATENT RIGHTS.

2.16 "BIOLOGICAL MATERIAL" means REGENTS':

[*]

3. GRANT

3.1 (a)Subject to the limitations set forth in this Agreement, including the license granted to the U.S. Government and the rights reserved in Paragraph 3.3, REGENTS hereby grants and LICENSEE hereby accepts an exclusive license under REGENTS' PATENT RIGHTS to develop, make, have made, use, offer for SALE, import, export, and SELL LICENSED PRODUCTS and LICENSED SERVICES, and to practice the LICENSED METHOD, in the LICENSED FIELD OF USE in the LICENSED TERRITORY.

(b) Subject to the limitations set forth in this Agreement and subject to the license granted to the U.S. Government, REGENTS hereby grants and LICENSEE hereby accepts an exclusive license under REGENTS' PROPERTY RIGHTS to possess, make and use, the BIOLOGICAL MATERIAL bailed to LICENSEE under this Agreement. LICENSEE acknowledges that the REGENTS is and will remain the sole owner of the BIOLOGICAL MATERIAL and the title of the material is not transferred to LICENSEE under this Agreement.

(c) REGENTS have provided the LICENSEE, one shipment of BIOLOGICAL MATERIAL in quantities that are deemed appropriate [*]. No additional obligation is required of REGENTS' with respect to bailment of the BIOLOGICAL MATERIAL.

3.2 The license under Paragraph 3.1 will be exclusive for a term commencing on the Effective Date and ending on the date of the last to expire patent under REGENTS' PATENT RIGHTS.

3.3 Nothing in this Agreement will be deemed to limit the right of REGENTS to publish any and all technical data resulting from any research performed by REGENTS relating to the INVENTIONS and the BIOLOGICAL MATERIAL. REGENTS expressly reserves the right to use the INVENTIONS, the BIOLOGICAL MATERIAL and related technology for its educational and research purposes; to disseminate the BIOLOGICAL MATERIAL and other tangible materials associated with, or required to practice the INVENTIONS and/or the REGENTS' PATENT RIGHTS to researchers at nonprofit institutions for their educational and research purposes and to permit other nonprofit institutions to use such BIOLOGICAL MATERIAL to practice the REGENTS' PATENT RIGHTS for education and research purposes.

3.4 This Agreement will terminate immediately if LICENSEE files a claim that includes, in any way, the assertion that any portion of the REGENTS' PATENT RIGHTS is invalid or unenforceable where the filing is by the LICENSEE, a third party on behalf of the LICENSEE (and with the actual knowledge of the LICENSEE), or a third party at the written urging of the LICENSEE.

3.5 LICENSEE will have a continuing responsibility to keep REGENTS informed of the large/small entity status, as defined in 15 U.S.C. 632, of itself and its sublicensees.

3.6 The INVENTIONS was funded in part by the U.S. Government. In accordance with PL 96-517 as amended by PL 98-620, to the extent required by law or regulation, any products covered by patent applications or patents claiming the INVENTIONS and sold in the United States will be substantially manufactured in the United States.

4. SUBLICENSES

4.1 REGENTS also grants to LICENSEE the right to sublicense to AFFILIATES and third parties the right to develop, make, have made, use, offer for SALE, import, export, and SELL LICENSED PRODUCTS and LICENSED SERVICES, and to practice LICENSED METHOD, provided that LICENSEE has exclusive rights

under this Agreement at the time of sublicensing. Every such sublicense will include:

(a) a statement setting forth the date upon which LICENSEE's exclusive rights, privileges, and license hereunder will expire;

(b) as applicable, all the rights of, and require the performance of all the obligations due to, REGENTS (and, if applicable, the United States Government) under this Agreement other than (i) any payment or reporting obligations (for which LICENSEE is directly responsible pursuant to Paragraph 4.6) and (ii) the indemnification obligation in Article 19 (which are addressed in Paragraph 4.1(d));

(c) a sublicensee shall have the right to grant further sublicense to its AFFILIATE and/or third parties to the extent sublicensee deems such sublicense is commercially reasonable, useful or necessary for the development and/or commercialization of LICENSED PRODUCT(S) or LICENSED METHOD(S) in accordance with this AGREEMENT; provided that (i) such sublicense is subject to a written sublicense agreement and is bound by all of the applicable terms, conditions, obligations, restrictions and other covenants of this AGREEMENT that protect or benefit the REGENTS'(and, if applicable, the U.S. Government's and other sponsors') rights and interests and (ii) sublicensee shall, within thirty (30) days after issuing any further sublicense, furnish to LICENSEE for delivery to REGENTS, subject to any confidentiality provisions with third parties, all material terms of any such sublicenses, pertaining to the REGENTS interests, including the sublicensee name and address; and Indemnification of REGENTS as provided in this AGREEMENT; and

(d) the same provision for indemnification of REGENTS as has been provided for in this Agreement.

4.2 LICENSEE will pay to REGENTS [*] of SUBLICENSE REVENUE.

In the event LICENSEE sublicenses the REGENTS' PATENT RIGHTS along with its own patent rights or those of other third parties, LICENSEE may reasonably determine in good faith the percentage of compensation received thereunder that represents consideration due for the grant of the rights under the REGENTS' PATENT RIGHTS, which percentage will be based upon the value of the

REGENTS' PATENT RIGHTS licensed to the sublicensee relative to the value of the other third party patent rights licensed to the sublicensee. When making payment under this Paragraph 4.2, LICENSEE shall provide REGENTS with all supporting information and documentation used to determine any such percentage (or shall reference previously provided supporting information and documentation). However, in no case will LICENSEE reduce the compensation to The REGENTS below [*] of the sublicensed patent rights.

[*]

4.3 LICENSEE will notify REGENTS of each sublicense granted hereunder and furnish to REGENTS a copy of each such sublicense agreement. Such copy may be redacted by LICENSEE to protect sensitive information. However, such copy shall contain sufficient information to assure REGENTS that the sublicense is consistent with this Agreement, and under no circumstances shall any financial terms necessary to calculate payments due to REGENTS hereunder be redacted.

4.4 AFFILIATES will have no licenses under REGENTS' PATENT RIGHTS except as granted by sublicense pursuant to this Agreement.

4.5 For the purposes of this Agreement, the operations of all sublicensees shall be deemed to be the operations of LICENSEE, for which LICENSEE shall be responsible.

4.6 LICENSEE will be responsible for payment of all monies and other consideration due REGENTS hereunder as a result of the activities of sublicensees, and all reports due REGENTS hereunder will reflect such activities.

4.7 Upon termination of this Agreement for any reason, all sublicenses that are granted by LICENSEE pursuant to this Agreement where the sublicensee is in compliance with its sublicense agreement as of the date of such termination will survive such termination (as a direct license(s) from REGENTS), provided that (a) each such direct license shall be subject to the same non-financial terms and conditions as those in this Agreement, except that REGENTS will not be bound to perform any duties or obligations set forth in any sublicenses that extend beyond the duties and obligations of REGENTS set forth in this Agreement; (b) such sublicensee (or if there is at such time more than one such sublicensee, such sublicensees severally and jointly) shall be required to make any annual maintenance payments due pursuant to Paragraph 5.2 or any minimum annual royalties due pursuant to

Paragraph 6.7; and (c) and such sublicensee shall be required to make any other monetary payment(s) that, had this Agreement not been terminated, LICENSEE would have been required to make under this Agreement as a result of the license to or activities of such sublicensee.

4.8 If REGENTS (to the extent of the actual knowledge of the licensing professional responsible for administration of this case) or a third party discovers and notifies that licensing professional that the INVENTIONS are useful for an application covered by the LICENSED FIELD OF USE, but for which LICENSED PRODUCTS have not been developed or are not currently under development by LICENSEE, and provided that such application does not compete, directly with LICENSED PRODUCTS that have been developed or are currently under development by LICENSEE (such application, the "NEW APPLICATION"), then REGENTS, as represented by the Office of Technology Licensing, shall give written notice to LICENSEE, except for: 1) information that is subject to restrictions of confidentiality with third parties, and 2) information which originates with REGENTS' personnel who do not assent to its disclosure to LICENSEE.

LICENSEE shall have [*] to give REGENTS written notice stating whether LICENSEE elects to develop LICENSED PRODUCTS for the NEW APPLICATION.

If LICENSEE elects to develop and commercialize the proposed LICENSED PRODUCTS for the NEW APPLICATION, LICENSEE shall submit progress reports to REGENTS pursuant to Article 8.

If LICENSEE elects not to develop and commercialize the proposed LICENSED PRODUCTS for use in the NEW APPLICATION, REGENTS may seek (a) third party(ies) to develop and commercialize the proposed LICENSED PRODUCTS for the NEW APPLICATION. If REGENTS is successful in finding a third party, it shall refer such third party to LICENSEE. If the third party requests a sublicense under this Agreement, then LICENSEE shall report the request to REGENTS within [*] from the date of such written request. If the request results in a sublicense, then LICENSEE shall report it to REGENTS pursuant to Paragraph 4.3. LICENSEE shall have no obligation to grant a sublicense to any third party under this Paragraph 4.8 (and, for clarity, the subsequent paragraph shall not apply) if such third party fails to request such sublicense within [*] after the expiration of the [*] period described above.

If LICENSEE refuses to grant a sublicense to the third party with respect to the NEW APPLICATION, then within [*] after such refusal LICENSEE shall submit to REGENTS a report specifying the license terms proposed by the third party and a written justification for LICENSEE's refusal to grant the proposed sublicense. If [*], then REGENTS shall have the right to grant to the third party a license to make, have made, use, sell, offer for sale and import products for use in the NEW APPLICATION [*].

5. LICENSE ISSUE FEE

5.1 LICENSEE will pay to REGENTS a non-creditable, non-refundable license issue fee of [*] due within thirty (30) days of the signing of the Agreement this fee is non-refundable and not an advance against royalties or other payments due under this Agreement.

5.2 LICENSEE will also pay to REGENTS an annual license maintenance fee of [*] beginning on the first anniversary of the Effective Date and on each anniversary of the Effective Date thereafter for the term of the AGREEMENT. Notwithstanding the foregoing, the license maintenance fee will not be due and payable on any anniversary of the Effective Date following the first SALE of a LICENSED PRODUCT, LICENSED METHOD OR LICENSED SERVICE.

6. ROYALTIES

6.1 LICENSEE will pay to REGENTS earned royalties at the rate of [*] of NET SALES, subject to the following:

(a) If LICENSEE is required to make any payment (including royalties or other license fees) to a third party to obtain a patent license or other patent rights in the absence of which LICENSEE could not practice REGENTS' PATENT RIGHTS, such third party payments [*] creditable against royalties owed hereunder by LICENSEE to REGENTS, provided that in no one calendar year will the total of such credits reduce earned royalties owed by LICENSEE to REGENTS by [*] on NET SALES of LICENSED PRODUCTS, LICENSED SERVICES and LICENSED METHODS.

(b) In the event a LICENSED PRODUCT, LICENSED SERVICE and LICENSED METHODS is, or LICENSED PRODUCTS, LICENSED

SERVICES and LICENSED METHODS are, combined with other licensed technologies for sales to end users by LICENSEE and the total combined royalty burden to LICENSEE on NET SALES exceeds [*], the earned royalty due to REGENTS will be adjusted, according to the following formula, where R is [*], C is [*] and B is the total combined royalty burden on LICENSEE:

Adjusted royalty = R x (C/B)

For example, if LICENSEE's total combined royalty is [*], the adjusted royalty due from LICENSEE to REGENTS would be calculated as [*] Notwithstanding the foregoing, in no event will the royalty due to REGENTS under this adjustment be less than [*].

(c) Only one royalty will be due on any given LICENSED PRODUCT, LICENSED METHOD and LICENSED SERVICE.

6.2 Royalties accruing to REGENTS will be paid to REGENTS quarterly within [*] after the end of each calendar quarter.

6.3 Royalties will be payable on SALES covered by a VALID CLAIM.

6.4 LICENSEE will pay to REGENTS milestone payments as follows:

i. For the first LICENSED PRODUCT or LICENSED METHOD, LICENSEE shall pay to REGENTS a milestone payment of [*] within [*] of the [*] and;

ii. For the first LICENSED PRODUCT or LICENSED METHOD, LICENSEE shall pay to REGENTS a milestone payment of [*] within [*] of the [*] and;

iii. LICENSEE will pay to REGENTS a milestone payment of [*] within [*] days of the [*] and;

iv. LICENSEE will pay to REGENTS a milestone payment of [*] within [*] of [*] and;

v. LICENSEE will pay to REGENTS a milestone payment of [*] within [*] of the [*] and;

vi. LICENSEE will pay to REGENTS a milestone payment of [*] within [*] of the [*] up to a maximum of two (2) additional indications.

vii. [*]

6.5 Beginning in the calendar year after the FIRST COMMERCIAL SALE and in each succeeding calendar year thereafter LICENSEE will pay to REGENTS a minimum annual royalty of [*] for the life of this Agreement. This minimum annual royalty will be paid to REGENTS by [*] of each year and will be credited against the earned royalty due and owing for the calendar year in which the minimum payment is made.

6.6 All payments due REGENTS will be payable in United States dollars. When LICENSED PRODUCTS, LICENSED SERVICES, or LICENSED METHOD are SOLD for monies other than United States dollars, earned royalties will first be determined in the foreign currency of the country in which the SALE was made and then converted into equivalent United States dollars. The exchange rate will be that rate quoted in [*] on the last business day of the reporting period.

6.7 Payments due for SALES occurring in any country outside the United States will not be reduced by any taxes, fees, or other charges imposed by the government of such country on the remittance of royalty income. LICENSEE will also be responsible for all bank transfer charges.

6.8 LICENSEE will make all payments under this Agreement by check payable to "The Regents of the University of California" and forward it to REGENTS at the address shown in Article 23 (Notices).

6.9 If any patent or patent application, or any claim thereof, included within REGENTS' PATENT RIGHTS expires or is held invalid in a final decision by a court of competent jurisdiction and last resort and from which no appeal has been or can be taken, all obligation to pay royalties based on such patent, patent application or claim, or any claims patentably indistinct therefrom will cease as of the date of such expiration or final decision. LICENSEE will not, however, be relieved from paying any royalties that accrued before such expiration or decision or that are based on another valid patent or claim not expired or involved in such decision.

6.10 No earned royalties will be collected or paid hereunder on SALES to, or for use by, the United States Government. LICENSEE will reduce the amount charged for such SALES by an amount equal to the earned royalty otherwise due REGENTS as provided herein.

7. DUE DILIGENCE

7.1 LICENSEE, upon execution of this Agreement, will diligently proceed with the development, manufacture, and SALE of LICENSED PRODUCTS, LICENSED SERVICES, and LICENSED METHOD, and will diligently market them in quantities sufficient to meet the market demand.

7.2 In addition to its obligations under Paragraph 7.1, LICENSEE specifically commits to achieving the following objectives in its due diligence activities under this Agreement:

(a) [*]

7.3 If LICENSEE is unable to meet any of its diligence obligations set forth in Paragraphs 7.1 and 7.2, then REGENTS will so notify LICENSEE of failure to perform. LICENSEE will have the right and option to extend the target date of any such due diligence obligation [*] upon the payment of [*] within thirty (30) days of the date to be extended for each such extension option exercised by LICENSEE. LICENSEE may further extend the target date of any diligence obligation for an additional [*] upon payment of an additional [*]. Additional extensions may be granted only by mutual written agreement of the parties to this Agreement. These payments are in addition to the minimum royalty payments specified in Paragraph 6.5. Should LICENSEE opt not to extend the obligation or fail to meet it by the extended target date, then REGENTS will have the right and option either to terminate this Agreement or to reduce LICENSEE's exclusive license to a non-exclusive royalty-bearing license, with all payments hereunder reduced to [*] of the royalties due under an exclusive license. This right, if exercised by REGENTS, supersedes the rights granted in Article 3. The right to terminate this Agreement or reduce LICENSEE's exclusive license granted hereunder to a non-exclusive license will be REGENTS' sole remedy for breach of Paragraph 7.1 or 7.2.

7.4 At the request of either party, any controversy or claim arising out of or relating to the diligence provisions of Paragraphs 7.1 and 7.2 will be settled by arbitration conducted in [*] in accordance with the then current [*]. Judgment upon the award rendered by the arbitrator(s) will be binding on the parties and may be entered by either party in the court or forum having jurisdiction. In determination of due diligence, [*].

7.5 To exercise either the right to terminate this Agreement or to reduce the license to a non-exclusive license for lack of diligence under Paragraph 7.1 or 7.2, REGENTS will give LICENSEE written notice of the deficiency. LICENSEE thereafter has [*] to cure the deficiency or to request arbitration. If REGENTS has not received a written request for arbitration or satisfactory tangible evidence that the deficiency has been cured by the end of the [*] period, then REGENTS may, at its option, either terminate the Agreement or reduce LICENSEE's exclusive license to a non-exclusive license, with all payments hereunder reduced to [*] of the royalties due under an exclusive license, by giving written notice to LICENSEE. These notices will be subject to Article 23 (Notices).

8. PROGRESS AND ROYALTY REPORTS

8.1 For the period beginning October 30, 2013, LICENSEE will submit to REGENTS a semi annual progress report covering LICENSEE's activities related to the development and testing of all LICENSED PRODUCTS, LICENSED SERVICES and LICENSED METHOD and the obtaining of necessary governmental approvals, if any, for marketing in the United States. These progress reports will be made for all development activities until the FIRST COMMERCIAL SALE occurs in the United States.

8.2 Each progress report will be a sufficiently detailed summary of activities of LICENSEE and any sublicensees so that REGENTS may evaluate and determine LICENSEE's progress in development of LICENSED PRODUCTS, LICENSED SERVICES, and LICENSED METHOD, and in meeting its diligence obligations under Article 7, and will include (but not be limited to) the following: summary of work completed and in progress; current schedule of anticipated events and milestones, including diligence milestones under Paragraph 7.2; anticipated market introduction dates for the licensed territories; and sublicensee's activities during the reporting period.

8.3 LICENSEE also will report to REGENTS in its immediately subsequent progress and royalty reports, the date of FIRST COMMERCIAL SALE.

8.4 After the FIRST COMMERCIAL SALE anywhere in the world, LICENSEE will make quarterly royalty reports to REGENTS within [*] after the quarters ending March 31, June 30, September 30, and December 31, of each year. Each such royalty report will include at least the following:

(a) The number of LICENSED PRODUCTS manufactured and the number SOLD;
(b) Gross revenue from SALE of LICENSED PRODUCTS, LICENSED SERVICES and LICENSED METHOD;
(c) NET SALES pursuant to Paragraph 2.5;
(d) Total royalties due REGENTS; and
(e) Names and addresses of any new sublicensees along with a summary of the material terms of each new sublicense agreement entered into during the reporting quarter.

8.5 If no SALES have occurred during the report period, a statement to this effect is required in the royalty report for that period.

9. BOOKS AND RECORDS

9.1 LICENSEE will keep full, true, and accurate books and records containing all particulars that may be necessary for the purpose of showing the amount of royalties payable to REGENTS and LICENSEE's compliance with other obligations under this Agreement. Said books and records will be kept at LICENSEE's principal place of business or the principal place of business of the appropriate division of LICENSEE to which this Agreement relates. Said books and records and the supporting data will be open at all reasonable times during normal business hours upon reasonable notice, for [*] following the end of the calendar year to which they pertain, to the inspection and audit by representatives of REGENTS for the purpose of verifying LICENSEE's royalty statement or compliance in other respects with this Agreement. Prior to any such inspection, such representatives will agree in a written agreement with LICENSEE to hold all information in confidence except as necessary to communicate LICENSEE's non-compliance with this Agreement to REGENTS.

9.2 The fees and expenses of REGENTS' representatives performing such an examination will be borne by REGENTS. However, if an error in underpaid royalties to REGENTS of [*] is discovered, then the fees and expenses of these representatives will be borne by LICENSEE.

10. LIFE OF THE AGREEMENT

10.1 Unless otherwise terminated by the operation of law or by acts of the parties in accordance with the terms of this Agreement, this Agreement will be in force from the Effective Date and will remain in effect for the life of the last-to-expire patent or last-to-be-abandoned patent application licensed under this Agreement, whichever is later.

10.2 Any termination of this Agreement shall not affect the rights and obligations set forth in the following articles:

Article 2	Definitions
Article 4	Sublicenses
Article 9	Books and Records
Article 10	Life of the Agreement
Article 13	Disposition of Licensed Products On Hand Upon Termination
Article 16	Use of Names and Trademarks
Article 17	Limited Warranties
Article 19	Indemnification
Article 23	Notices
Article 24	Late Payments
Article 26	Confidentiality
Article 29	Applicable Law; Venue; Attorneys' Fees

10.3 Any termination of this Agreement will not relieve LICENSEE of its obligation to pay any monies due or owing at the time of such termination and will not relieve any obligations, of either party to the other party, established prior to termination.

11. TERMINATION BY REGENTS

11.1 If LICENSEE should violate or fail to perform any term of this Agreement, then REGENTS may give written notice of such default ("Notice of Default") to LICENSEE. If LICENSEE should fail to repair such default within sixty (60) days of the effective date of such notice, REGENTS will have the right to terminate this Agreement and the licenses herein by a second written notice ("Notice of Termination") to LICENSEE. If a Notice of Termination is sent to LICENSEE, this Agreement will automatically terminate on the effective date of such notice. Such

termination will not relieve LICENSEE of its obligation to pay any royalty or license fees owing at the time of such termination and will not impair any accrued rights of REGENTS. These notices will be subject to Article 23 (Notices).

12. TERMINATION BY LICENSEE

12.1 LICENSEE will have the right at any time to terminate this Agreement in whole or as to any portion of REGENTS' PATENT RIGHTS by giving notice in writing to REGENTS. Such notice of termination will be subject to Article 23 (Notices) and termination of this Agreement will be effective (30) days after the effective date of such notice.

12.2 Any termination pursuant to Paragraph 12.1 will not relieve LICENSEE of any obligation or liability accrued hereunder prior to such termination or rescind anything done by LICENSEE or any payments made to REGENTS hereunder prior to the time such termination becomes effective, and such termination will not affect in any manner any rights of REGENTS arising under this Agreement prior to such termination.

13. DISPOSITION OF LICENSED PRODUCTS ON HAND UPON TERMINATION

13.1 Upon termination of this Agreement, for a period of [*] days after the date of termination LICENSEE may complete and SELL any partially made LICENSED PRODUCTS and continue to render any previously commenced LICENSED SERVICES, and continue the practice of LICENSED METHOD only to the extent necessary to do so; provided, however, that all such SALES will be subject to the terms of this Agreement including, but not limited to, the payment of royalties at the rate and at the time provided herein and the rendering of reports thereon. Upon termination of this Agreement by either party, LICENSEE shall return or destroy the BIOLOGICAL MATERIAL in its possession [*] following the effective date of termination, subject, however, to any continuing rights LICENSEE may have pursuant to any material transfer agreement between LICENSEE and REGENTS with respect to the BIOLOGICAL MATERIAL. Subject to such exception, LICENSEE shall provide REGENTS [*] following said termination date with written notice that the BIOLOGICAL MATERIAL has been returned or destroyed.

14. PATENT PROSECUTION AND MAINTENANCE

14.1 REGENTS will diligently prosecute and maintain the United States and foreign patent applications and patents under REGENTS' PATENT RIGHTS, subject to LICENSEE'S reimbursement REGENTS' out of pocket costs under Article 14.3 below, and all patent applications and patents under REGENTS' PATENT RIGHTS will be held in the name of REGENTS. REGENTS will have sole responsibility for retaining and instructing patent counsel, but continued use of such counsel at any point in the patent prosecution process subsequent to initial filing of a U.S. patent application covering the INVENTIONS shall be subject to the approval of LICENSEE. If LICENSEE rejects three of REGENTS' choice of prosecution counsel, then REGENTS may select new prosecution counsel without LICENSEE's consent. REGENTS shall promptly provide LICENSEE with copies of all relevant documentation so that LICENSEE may be currently informed and apprised of the continuing prosecution and LICENSEE agrees to keep this documentation confidential in accordance with Article 26. LICENSEE may comment upon such documentation, provided, however, that if LICENSEE has not commented upon such documentation in reasonable time for REGENTS to sufficiently consider LICENSEE's comments prior to the deadline for filing a response with the relevant government patent office, REGENTS will be free to respond appropriately without consideration of LICENSEE's comments. LICENSEE and LICENSEE's patent counsel will have the right to consult with patent counsel chosen by REGENTS.

14.2 REGENTS will use reasonable efforts to prepare or amend any patent application to include claims reasonably requested by LICENSEE to protect the LICENSED PRODUCTS contemplated to be SOLD or to be practiced under this Agreement.

14.3 Subject to Paragraph 14.4, all past, present, and future costs for preparing, filing, prosecuting, and maintaining all United States and foreign patent applications, and patents under REGENTS' PATENT RIGHTS will be borne by LICENSEE, so long as the licenses granted to LICENSEE herein are exclusive. To date the remaining past patent costs paid by REGENTS are about [*]. Payments are due within thirty (30) days after receipt of invoice from REGENTS. If, however, REGENTS reduces the exclusive licenses granted herein to non-exclusive licenses pursuant to Paragraphs 7.3, 7.4, or 7.5 and REGENTS grants additional license(s), the costs of preparing, filing, prosecuting and maintaining such patent applications and patents

will be divided equally among the licensed parties from the effective date of each subsequently granted license agreement.

14.4 LICENSEE's obligation to underwrite and to pay all domestic and foreign patent filing, prosecution, and maintenance costs will continue for so long as this Agreement remains in effect, provided, however, that LICENSEE may terminate its obligations with respect to any given patent application or patent in any or all designated countries upon [*] written notice to REGENTS. REGENTS will use its best efforts to curtail patent costs when such a notice is received from LICENSEE. REGENTS may continue prosecution and/or maintenance of such applications or patents at its sole discretion and expense; provided, however, that LICENSEE will have no further right or licenses thereunder.

15. MARKING

15.1 Prior to the issuance of patents under REGENTS' PATENT RIGHTS, LICENSEE agrees to mark LICENSED PRODUCT(S) (or their containers or labels) made, sold, licensed or otherwise disposed of by it in the United States under the license granted in this Agreement with the words "Patent Pending," and following the issuance in the United States of one or more patents under REGENTS' PATENT RIGHTS, with the numbers of the REGENTS' PATENT RIGHTS. All LICENSED PRODUCTS shipped to, manufactured, or sold in other countries will be marked in such manner as to conform with the patent laws and practice of such countries.

16. USE OF NAMES AND TRADEMARKS

16.1 Nothing contained in this Agreement will be construed as conferring any right to use in advertising, publicity or other promotional activities any name, trademark, trade name, or other designation of either party hereto by the other (including any contraction, abbreviation, or simulation of any of the foregoing). Unless required by law or consented to in writing by REGENTS, the use by LICENSEE of the name "The Regents of the University of California" or the name of any University of California campus in advertising, publicity or other promotional activities is expressly prohibited. Unless required by law or consented to in writing by LICENSEE, the use by REGENTS of the name "Avalanche Biotechnologies" in advertising, publicity or other promotional activities is expressly prohibited.

17. LIMITED WARRANTIES

17.1 REGENTS warrants to LICENSEE that it has the lawful right to grant this license.

17.2 To the extent of the actual knowledge of the licensing professional responsible for administration of the Agreement as of the Effective Date, it is the owner of the REGENT'S PATENT RIGHTS, and it has not granted any right, license or interest in or to the REGENT'S PATENT RIGHTS to any third party.

17.3 Except as provided herein, this license, the BIOLOGICAL MATERIAL and the associated INVENTIONS are provided WITHOUT WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESSED OR IMPLIED. REGENTS MAKES NO REPRESENTATION OR WARRANTY THAT THE INVENTIONS, THE BIOLOGICAL MATERIAL, REGENTS' PATENT RIGHTS, LICENSED PRODUCTS, LICENSED SERVICES OR LICENSED METHOD WILL NOT INFRINGE ANY PATENT OR OTHER PROPRIETARY RIGHT.

17.4 EXCEPT OF LICENSEE'S DUTIES FOR CLAIMS OF THIRD PARTIES UNDER ARTICLE 19, IN NO EVENT WILL EITHER PARTY BE LIABLE TO THE OTHER FOR ANY INCIDENTAL, SPECIAL OR CONSEQUENTIAL DAMAGES RESULTING FROM EXERCISE OF THIS LICENSE OR THE USE OF THE INVENTIONS, THE BIOLOGICAL MATERIAL, REGENTS' PATENT RIGHTS, LICENSED METHOD, LICENSED SERVICES OR LICENSED PRODUCTS.

17.5 Except as expressly provided in this Article 17, nothing in this Agreement is or will be construed as:

(a) A warranty or representation by REGENTS as to the validity, enforceability or scope of any REGENTS' PATENT RIGHTS; or

(b) A warranty or representation that anything made, used, or SOLD under any license granted in this Agreement is or will be free from infringement of patents of third parties; or

(c) An obligation to bring or prosecute actions or suits against third parties for patent infringement, except as provided in Article 18; or

(d) Conferring by implication, estoppel, or otherwise any license or rights under any patents of REGENTS other than REGENTS' PATENT RIGHTS as defined herein, regardless of whether such patents are dominant or subordinate to REGENTS' PATENT RIGHTS; or

(e) An obligation to furnish any know-how not provided in the patents and patent applications under REGENTS' PATENT RIGHTS, and REGENTS' PROPERTY RIGHTS as defined herein.

18. PATENT INFRINGEMENT

18.1 In the event that a party (in the case of the REGENTS to the extent of the actual knowledge of the licensing professional responsible for the administration of this Agreement) learns of the substantial infringement of any REGENTS' PATENT RIGHTS under this Agreement, such party will promptly provide the other party with notice and reasonable evidence of such infringement ("Infringement Notice"). During the period and in a jurisdiction where LICENSEE has exclusive rights under this Agreement, neither party will notify a third party, including the infringer, of the infringement without first obtaining consent of the other party, which consent will not be unreasonably withheld. Both parties will use diligent efforts, in cooperation with each other, to terminate such infringement without litigation.

18.2 LICENSEE shall have the first right to institute suit for patent infringement against the infringer [*] after the Infringement Notice in 18.1. REGENTS may voluntarily join such suit at its own expense, but may not thereafter commence suit against the infringer for the acts of infringement that are the subject of LICENSEE's suit or any judgment rendered in that suit. LICENSEE may not join REGENTS in a suit initiated by LICENSEE without REGENTS' prior written consent. If, in a suit initiated by LICENSEE, REGENTS is involuntarily joined other than by LICENSEE, LICENSEE will pay any third party costs incurred by REGENTS arising out of such suit, including but not limited to, any legal fees of outside counsel that REGENTS selects and retains to represent it in the suit.

If, within [*] following the effective date of the Infringement Notice, the infringing activity of potential commercial significance has not been abated and if LICENSEE has not brought suit against the infringer, REGENTS may institute suit for patent infringement against the infringer. If REGENTS institutes such suit, LICENSEE may not join such suit without REGENTS' consent and may not thereafter commence suit against the infringer for the acts of infringement that are the subject of REGENTS' suit or any judgment rendered in that suit.

18.3 Such legal action as is decided upon will be at the expense of the party on account of whom suit is brought and all recoveries recovered thereby will belong to such

party, provided that legal action brought jointly by REGENTS and LICENSEE and participated in by both, will be at the joint expense of the parties and all recoveries will be allocated in the following order: a) to each party reimbursement in equal amounts of the attorney's costs, fees, and other related expenses to the extent each party paid for such costs, fees, and expenses until all such costs, fees, and expenses are consumed for each party; and b) any remaining amount shared jointly by them in proportion to the share of expenses paid by each party, but in no event will REGENTS' share be [*] of such remaining amount if REGENTS is a party.

18.4 Each party will cooperate with the other in litigation instituted hereunder but at the expense of the party on account of whom suit is brought. Such litigation will be controlled by the party bringing the action, except that REGENTS may be represented by counsel of its choice in any suit brought by LICENSE.

18.5 Any agreement made by LICENSEE for the purposes of settling litigation or other dispute shall comply with the requirements of Article 4 (Sublicenses) of this Agreement.

19. INDEMNIFICATION

19.1 LICENSEE will, and will require its sublicensees to, indemnify, hold harmless, and defend REGENTS and its officers, employees, and agents; sponsor(s) of the research that led to the INVENTIONS; and BIOLOGICAL MATERIAL covered by REGENTS' PROPERTY RIGHTS; and the inventors of any patents and patent applications under REGENTS' PATENT RIGHTS and their employers against any and all claims, suits, losses, damages, costs, fees, and expenses resulting from or arising out of exercise of this license or any sublicense or any use or possession of the BIOLOGICAL MATERIAL. This indemnification will include, but not be limited to, any product liability.

19.2 LICENSEE, at its sole cost and expense, will insure its activities in connection with any work performed hereunder and will obtain, keep in force, and maintain the following insurance:

(a) Commercial Form General Liability Insurance (contractual liability included) with limits as follows:

Each Occurrence [*]
Products/Completed Operations Aggregate [*]

Personal and Advertising Injury [*]
General Aggregate [*]

If the above insurance is written on a claims-made form, it shall continue for [*] years following termination or expiration of this Agreement. The insurance shall have a retroactive date of placement prior to or coinciding with the Effective Date of this Agreement; and

(b) Worker's Compensation as legally required in the jurisdiction in which LICENSEE is doing business.

19.3 The coverage and limits referred to in Subparagraphs 19.2a and 19.2b above will not in any way limit the liability of LICENSEE under this Article. Upon the execution of this Agreement, LICENSEE will furnish REGENTS with certificates of insurance evidencing compliance with all requirements. Such certificates will:

(a) provide for [*] advance written notice to REGENTS of any cancellation of insurance coverages; LICENSEE will promptly notify REGENTS of any material modification of the insurance coverages;

(b) indicate that REGENTS has been endorsed as an additional insured under the coverage described above in Subparagraph l9.2; and

(c) include a provision that the coverage will be primary and will not participate with, nor will be excess over, any valid and collectable insurance or program of self-insurance maintained by REGENTS.

19.4 REGENTS will promptly notify LICENSEE in writing of any claim or suit brought against REGENTS for which REGENTS intends to invoke the provisions of this Article 19. LICENSEE will keep REGENTS informed of its defense of any claims pursuant to this Article 19.

20. COMPLIANCE WITH LAWS

20.1 LICENSEE will comply with all applicable international, national, state, regional, and local laws and regulations in performing its obligations hereunder and in its use, manufacture, SALE or import of the LICENSED PRODUCTS, LICENSED SERVICES, or practice of the LICENSED METHOD. LICENSEE understands that REGENTS is subject to United States laws and regulations (including the Arms

Export Control Act, as amended, and the Export Administration Act of 1979), controlling the export of technical data, computer software, laboratory prototypes and other commodities, and REGENTS' obligations under this Agreement are contingent on compliance with such laws and regulations. The transfer of certain technical data and commodities may require a license from the cognizant agency of the United States Government and/or written assurances by LICENSEE that LICENSEE will not export such technical data and/or commodities to certain foreign countries without prior approval of such agency. REGENTS neither represents that a license will not be required nor that, if required, it will be issued.

21. GOVERNMENT APPROVAL OR REGISTRATION

21.1 If this Agreement or any associated transaction is required by the law of any nation to be either approved or registered with any governmental agency, LICENSEE will assume all legal obligations to do so. LICENSEE will notify REGENTS if it becomes aware that this Agreement is subject to a United States or foreign government reporting or approval requirement. LICENSEE will make all necessary filings and pay all costs including fees, penalties, and all other out-of-pocket costs associated with such reporting or approval process.

22. ASSIGNMENT

22.1 This Agreement is binding upon and shall inure to the benefit of REGENTS, its successors and assigns. This Agreement will be personal to LICENSEE and assignable by LICENSEE only with the written consent of REGENTS, except that LICENSEE may freely assign this Agreement to an acquirer of all or substantially all of LICENSEE's stock, assets or business.

23. NOTICES

23.1 All notices under this Agreement will be deemed to have been fully given and effective when done in writing and delivered in person, or mailed by registered or certified U.S. mail, or deposited with a carrier service requiring signature by recipient, and addressed as follows:

To REGENTS: Office of Technology Licensing
2150 Shattuck Avenue, Suite 510

Berkeley, CA 94704-1347
Attn.: Director [*]

To LICENSEE: Avalanche Biotechnologies, Inc
665 Third Street, Suite 250
San Francisco, CA 94107
Attn.: Thomas W. Chalberg, Ph.D.

Either party may change its address upon written notice to the other party.

24. LATE PAYMENTS

24.1 If monies owed to REGENTS under this Agreement are not received by REGENTS when due, LICENSEE will pay to REGENTS interest charges [*] on the date such payment is due, [*]. Such interest will be calculated from the date payment was due until actually received by REGENTS. Such accrual of interest will be in addition to, and not in lieu of, enforcement of any other rights of REGENTS related to such late payment. Acceptance of any late payment will not constitute a waiver under Article 25 (Waiver) of this Agreement.

25. WAIVER

25.1 The failure of either party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement will not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other party. None of the terms and conditions of this Agreement can be waived except by the written consent of the party waiving compliance.

26. CONFIDENTIALITY

26.1 Each party will hold the other party's proprietary business and technical information, patent prosecution material and other proprietary information, including the negotiated terms of this Agreement, in confidence and against disclosure to third parties with at least the same degree of care as it exercises to protect its own data and license agreements of a similar nature. This obligation will expire [*] years after the termination or expiration of this Agreement.

26.2 Nothing contained herein will in any way restrict or impair the right of LICENSEE or REGENTS to use, disclose, or otherwise deal with any information or data which:

(a) at the time of disclosure to a receiving party is generally available to the public or thereafter becomes generally available to the public by publication or otherwise through no act of the receiving party;

(b) the receiving party can show by written record was in its possession prior to the time of disclosure to it hereunder and was not acquired directly or indirectly from the disclosing party; or

(c) is independently made available to the receiving party without restrictions as a matter of right by a third party.

In addition, nothing contained herein will in any way restrict or impair the right of LICENSEE or REGENTS to make any disclosure required under the California Public Records Act or pursuant to other requirements of law.

26.3 REGENTS will be free to release to the inventors and senior administrators employed by REGENTS the terms and conditions of this Agreement upon their request. If such release is made, REGENTS will inform such employees of the confidentiality obligations set forth above and will request that they do not disclose such terms and conditions to others. Should a third party inquire whether a license to REGENTS' PATENT RIGHTS is available, REGENTS may disclose the existence of this Agreement and the extent of the grant in Articles 3 and 4 to such third party, but will not disclose the name of LICENSEE unless LICENSEE has already made such disclosure publicly, except where REGENTS is required to release information under either the California Public Records Act or other applicable law, provided REGENTS gives prior written notice to LICENSEE of such disclosure.

26.4 LICENSEE and REGENTS agree to destroy or return to the disclosing party proprietary information received from the other in its possession within fifteen (15) days following the effective date of termination of this Agreement. However, each party may retain one copy of proprietary information of the other solely for archival purposes in non-working files for the sole purpose of verifying the ownership of the proprietary information, provided such proprietary information will be subject to the confidentiality provisions set forth in Article 26.1. LICENSEE and REGENTS agree to provide each other, within thirty (30) days following

termination of this Agreement, with a written notice that proprietary information has been returned or destroyed.

27. FORCE MAJEURE

27.1 Except for LICENSEE's obligation to make any payments to REGENTS hereunder, the parties to this Agreement shall be excused from any performance required hereunder if such performance is rendered impossible or unfeasible due to any catastrophes or other major events beyond their reasonable control, including, without limitation, war, riot, and insurrection; laws, proclamations, edicts, ordinances, or regulations; strikes, lockouts, or other serious labor disputes; and floods, fires, explosions, or other natural disasters. When such events have abated, the parties' respective obligations hereunder will resume.

28. SEVERABILITY

28.1 The provisions of this Agreement are severable, and in the event that any provision of this Agreement will be determined to be invalid or unenforceable under any controlling body of law, such invalidity or enforceability will not in any way affect the validity or enforceability of the remaining provisions hereof.

29. APPLICABLE LAW; VENUE; ATTORNEYS' FEES

29.1 THIS AGREEMENT WILL BE CONSTRUED, INTERPRETED, AND APPLIED IN ACCORDANCE WITH THE LAWS OF THE STATE OF CALIFORNIA, excluding any choice of law rules that would direct the application of the laws of another jurisdiction, but the scope and validity of any patent or patent application under REGENTS' PATENT RIGHTS will be determined by the applicable law of the country of such patent or patent application. Any legal action brought by the parties relating to this Agreement will be conducted in [*]. The prevailing party in any legal action under this Agreement will be entitled to recover its reasonable attorneys' fees in addition to its costs and necessary disbursements.

30. ELECTRONIC COPY

30.1 The parties to this document agree that a copy of the original signature (including an electronic copy) may be used for any and all purposes for which the original

signature may have been used. The parties further waive any right to challenge the admissibility or authenticity of this document in a court of law based solely on the absence of an original signature.

31. SCOPE OF AGREEMENT

31.1 This Agreement (except for the Confidentiality Agreement [*] which will continue to the extent it is not inconsistent with this Agreement) incorporates the entire agreement between the parties with respect to the subject matter hereof, and this Agreement may be altered or modified only by written amendment duly executed by the parties hereto.

[*] = 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.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

THE REGENTS OF THE
UNIVERSITY OF CALIFORNIA

By /s/ Carol Mimura
Carol Mimura, Ph.D.
Assistant Vice Chancellor
Office of Technology Licensing

Date

AVALANCHE BIOTECHNOLOGIES, INC.

By/s/ Thomas Chalberg
Thomas Chalberg, Ph.D.
Chief Executive Officer

DateJune 17, 2013

[*] = 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.

[*] = 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 10.47

LICENSE AGREEMENT

This License Agreement (the "**Agreement**") dated October 12, 2011 (the "**Effective Date**"), is between **Virovek, Inc.**, a Delaware corporation ("**Virovek**") with an address at 3521 Investment Boulevard, Suite 1, Hayward, California 94545, **and Avalanche Biotechnologies, Inc.**, a Delaware corporation ("**Avalanche**") with an address at 665 Third Street, Suite 250, San Francisco, California 94107. Virovek and Avalanche shall each be a "**Party**" and together shall be the "**Parties**".

Recitals

Whereas, Virovek has developed proprietary methods and materials for manufacturing adeno-associated virus ("**AAV**") using baculovirus;

Whereas, Avalanche is a drug delivery company that specializes in the development of novel therapeutics for the treatment of ophthalmic diseases and conditions;

Whereas, Virovek and Avalanche desire to enter into a license agreement pursuant to which Avalanche would receive rights to use and further develop Virovek's proprietary technology for the production of clinical and commercial scale quantities of Avalanche's proprietary therapeutic products; and

Whereas, Virovek will also grant to Avalanche the right to develop, use and commercialize, itself or with or through third parties, Virovek's proprietary technology for the production of other therapeutic products at clinical and commercial scale;

Now, Therefore, in consideration of the foregoing premises and the mutual covenants below, the Parties agree as follows:

ARTICLE 1

DEFINITIONS

The following terms, whenever used in this Agreement, shall have the following meanings:

1.1 "**Affiliate**" means any entity that directly or indirectly controls, is controlled by or is under common control with the Party and for this purpose "control" means the possession directly or indirectly of the power to direct or cause the direction of the management and policies of the entity whether through voting shares, securities or otherwise.

1.2 "**Applicable Laws**" shall mean all federal, state and local laws statutes, rules, regulations, and ordinances, applicable to the development, manufacture, distribution, use and

Commercialization of Licensed Products throughout the world including without limitation, the applicable regulations and guidelines of any governmental authority including the FDA and foreign counterparts and all applicable good manufacturing practices together with amendments thereto.

1.3 "**Audit Trigger**" means the date upon which Avalanche becomes obligated to pay to Virovek pursuant to this Agreement an aggregate of [*]

1.4 "**Avalanche Product**" means a Licensed Product, whether it is a Standard Product or an Improved Product, that (i) is developed in whole or in part by Avalanche or its Affiliates, alone or with their Sublicensees, and (ii) incorporates any composition of matter potentially useful for the prevention, treatment or amelioration of a disease or condition, and/or is based on a method of treatment or use, that is covered by intellectual property rights controlled by Avalanche or its Affiliates other than those licensed to Avalanche by Virovek pursuant to this Agreement.

1.5 "**Calendar Quarter**" means each three month period commencing on the first day of January, April, July and October in any given calendar year.

1.6 "**Combination Product**" means a product that includes an Avalanche Product and at least one (1) Other Component.

1.7 "**Commercialize**" means to use commercially, sell, have sold, offer for sale, market, promote, import, export or otherwise exploit a Licensed Product.

1.8 "**Confidential Information**" means all non-publicly available information provided by one Party to the other Party, including without limitation any information that relates to the Licensed Product, or any gene sequences, genetic mutations, variations or polymorphisms, vectors, organisms, cells, cell lines, tissues, biochemical or physiological consequences of any genetic variation, research, technology, discoveries, data, inventions, assays, production processes, know-how, products, services, clients, partners, markets, employees, business plans and financial information.

1.9 "**Control**" or "**Controlled**" means, with respect to any designated item or intellectual property right with respect to which a right or license is granted by a Party to the other hereunder, the ability and right (whether by ownership or license, other than pursuant to this Agreement) of the Party to grant such right or license as provided for herein without violating the terms of any agreement or other arrangement with any Third Party existing at the time such Party grants the other Party such right or license.

1.10 "**FDA**" means the U.S. Food and Drug Administration of the U.S. Department of Health and Human Services and any successor agencies.

1.11 "**Field**" means all fields of use.

1.12 "**Improved Product**" means any Licensed Product incorporating or otherwise produced utilizing (i) technology or intellectual property that is Controlled by Avalanche (other than a Virovek Improvement) in addition to [*] or (ii) any Improvements conceived and reduced to practice in whole or in part by Avalanche following the Effective Date.

1.13 "**Improvements**" means any modification, development, enhancement, derivative, variation or improvement to the Virovek Technology, including, without limitation, a composition of matter, a method of making or using, a formulation, a configuration or other attribute of the materials, organisms, methods, media, production process flow, downstream processing and/or scaleability, or other items used to practice the Virovek Technology as it exists as of the Effective Date or as it is improved in the course of the Parties' activities under this Agreement that is made by either Party in performing activities under this Agreement.

1.14 "**Know-How**" shall mean any and all Confidential Information, trade secrets, technology, media, materials, samples, know-how, show-how, discoveries, algorithms, unpatented inventions, developments, improvements, techniques, methods, test methods, processes, protocols, recipes, data (including development data), instructions, formulae, drawings and specifications, whether or not patentable or protectable.

1.15 "**Law**" shall mean any federal, state or local law, statute or ordinance, or any rule, regulation, or published guidelines promulgated by any governmental or Regulatory Authority in any jurisdiction.

1.16 "**Licensed Product**" means any product that is made using or that incorporates the Virovek Technology (including any Virovek know-how) and/or a Virovek Improvement. For the avoidance of doubt, Licensed Products include Standard Products or Improved Products that incorporate Virovek Technology and/or Virovek Improvements, but shall not include products that do not incorporate any Virovek Technology or Virovek Improvements.

1.17 "**Net Sales**" means the gross amount invoiced by or on behalf of Avalanche, its Affiliates and their respective Sublicensees for sales of Avalanche Products in the Territory (other than sales among Avalanche, its Affiliates or Sublicensees for subsequent resale, in which case the first sale to a Third Party that is not a Sublicensee or an Affiliate of a Sublicensee shall be used for calculation of Net Sales), less the following deductions if and to the extent they are (i) included in the gross invoiced sales price of Avalanche Products or otherwise directly incurred by Avalanche, its Affiliates and their respective Sublicensees with respect to the sale of Avalanche Products, and (ii) not otherwise deducted in computing other amounts hereunder: (a) Voluntary rebates, quantity and cash discounts, and other discounts to customers, [*] (b) taxes (except income taxes) and tariffs or duties paid, absorbed or allowed which are directly related to the sale of Avalanche Products, (c) credits, allowances, discounts and rebates to, and chargebacks for, spoiled, damaged, out-dated, rejected or returned Avalanche Products (including in connection with Avalanche Product withdrawals, expired Avalanche Product and Avalanche Product recalls), (d) actual freight and insurance costs, including without limitation the costs of export licenses, shipping, postage and handling charges, incurred in transporting Avalanche Products to customers, (e) discounts, retroactive price reductions, rebates or other payments required by government entities, government regulations, or Applicable Law, including any governmental medical assistance programs, and (f) customs duties, surcharges and other governmental charges incurred in connection with the exportation or importation of Avalanche Products.

In the case of any sale or other disposal of Product for non-cash consideration, Net Sales shall be calculated as the fair market price of Avalanche Products in the country of sale or disposal. Notwithstanding the foregoing, provision of Avalanche Products for the purpose of conducting

pre-clinical or clinical research shall not be deemed to be a sale. For clarity, any Avalanche Products provided as free samples or as charitable donations shall not give rise to any Net Sales. Net Sales shall be determined in accordance with GAAP.

Notwithstanding the foregoing, in the event a Product is sold in a country in the Territory as a Combination Product, Net Sales of the Combination Product will be calculated as follows:

(i) If the Avalanche Product contained in the Combination Product and Other Component(s) contained in the Combination Product each are sold separately in such country, Net Sales will be calculated by multiplying the total Net Sales (as described above) of the Combination Product by the fraction A/(A+B), where A is the [*] in such country of the Avalanche Product sold separately in the same formulation and dosage, and B is the sum of the [*] in such country of such Other Component(s) sold separately in the same formulation and dosage, during the applicable Calendar Year.

(ii) If the Avalanche Product contained in the Combination Product is sold independently of the Other Component(s) contained in the Combination Product in such country, but the average gross selling price of such Other Component(s) in such country cannot be determined, Net Sales will be calculated by multiplying the total Net Sales (as described above) of the Combination Product by the fraction A/C where A is the [*] in such country of such Avalanche Product sold independently and C is the [*] in such country of the entire Combination Product, during the applicable Calendar Year.

(iii) If the Other Component(s) contained in the Combination Product are sold independently of the Avalanche Product contained in the Combination Product in such country, but the average gross selling price of such Avalanche Product in such country cannot be determined, Net Sales will be calculated by multiplying the total Net Sales (as described above) of the Combination Product by the fraction (1-(B/C)), where B is the [*] in such country of such Other Component(s) and C is the [*] in such country of the entire Combination Product, during the applicable Calendar Year.

(iv) If the Avalanche Product contained in the Combination Product and Other Component(s) contained in the Combination Product are not sold separately in such country, or if they are sold separately but the average gross selling price of neither such Avalanche Product nor such Other Component(s) can be determined in such country, Net Sales of the Combination Product in such country will be [*]

1.18 "**Other Component**" means, for purposes of Section 1.16, any therapeutically active pharmaceutical ingredient or delivery device other than an Avalanche Product.

1.19 "**Other Products**" means any Licensed Product, whether it is a Standard Product or an Improved Product, that is not an Avalanche Product.

1.20 "**Patents**" means (a) unexpired letters patent (including without limitation inventor's certificates), including without limitation any substitution, extension, registration, confirmation, reissue, re-examination, renewal, or any like filing thereof ("**Issued Patents**"), and (b) pending applications for letters patent, including without limitation any continuation,

divisional, or continuation-in-part thereof, and any provisional or non-provisional applications ("**Patent Applications**").

1.21 "**Regulatory Authority**" means the FDA in the United States, and the equivalent regulatory authority or governmental entity having the responsibility, jurisdiction, and authority to approve the manufacture, use, importation, packaging, labeling, marketing, and sale of diagnostic products in any country or jurisdiction in the Territory other than the United States.

1.22 "**Standard Product**" means any Licensed Product incorporating or otherwise produced utilizing technology disclosed in the Initial Patent Application as it exists as of the Effective Date, or any Virovek Improvement, but not any (i) technology or intellectual property that is Controlled by Avalanche in addition to that disclosed in the Initial Patent Application (other than a Virovek Improvement), or (ii) any Improvements conceived and reduced to practice by Avalanche following the Effective Date.

1.23 "**Sublicensee**" means an Affiliate of Avalanche or a Third Party to which a sublicense is granted under the license granted to Avalanche in Section 2.1, in accordance with Section 2.3 and/or 2.4, including any Affiliate of Avalanche or Third Party that receives a further sublicense from another such Affiliate or Third Party sublicense.

1.24 "**Technology Transfer**" means the transfer from Virovek to Avalanche, its Affiliates or its Sublicensees of the Licensed Know-How as provided in Section 7.1.

1.25 "**Territory**" means worldwide.

1.26 "**Third Party Revenue**" means all consideration received by Avalanche in consideration for the grant of a sublicense under the rights granted to Avalanche pursuant to Section 2.1 with respect to Other Products, excluding (i) equity investments made by Sublicensees in Avalanche, to the extent such investments do not exceed the fair market value of such equity, (ii) payment by Sublicensees to Avalanche as reimbursement of patent expenses or expenses related to Technology Transfer or technical support, in each case related to Other Products, (iii) payments by Sublicensees to Avalanche for research, development, and pre-clinical and clinical studies undertaken by Avalanche on behalf of Sublicensees or financing of research and development at Avalanche's expense related to Other Products, (iv) payments for the supply of Other Products, or components and materials used for the production of Other Products, and (v) amounts received in consideration for intellectual property rights that are not Virovek Patents or Virovek Know-How, as reasonably determined by Avalanche.

1.27 "**Third Party**" means any entity other than Avalanche or Virovek, or an Affiliate of either of them.

1.28 "**Valid Claim**" means for any country, a claim of an Issued Patent that has not expired or been held unpatentable, invalid, or unenforceable by a court or other government agency of competent jurisdiction in an unappealed or unappealable decision or has not been admitted to be invalid or unenforceable through reissue, re-examination, disclaimer, or otherwise, or a claim of a Patent Application that has been filed in good faith and not abandoned or withdrawn, and which has not been pending before the applicable patent office for a period [*] from the original

date of filing, provided that if a pending Patent Application becomes an Issued Patent at any time after the expiration of such [*] period, the claims of such Issued Patent shall be Valid Claims from the date upon which they issue.

1.29 "**Virovek Improvement**" means any Improvement created or reduced to practice (either actually or constructively in a Patent Application or Issued Patent) solely by Virovek.

1.30 "**Virovek Know-How**" means all Know-How Controlled by Virovek that is necessary or useful for the development, manufacture, use or Commercialization of Licensed Product, or otherwise for the practice of the Virovek Technology in the Field, including without limitation any technical data and characterizing specifications for the Standard Product or any Improved Product that is not publically available.

1.31 "**Virovek Patents**" means all Patents Controlled by Virovek claiming inventions that are necessary or useful for the development, manufacture, use or Commercialization of Licensed Products, or otherwise for the practice of the Virovek Technology in the Field, [*] (the "**Initial Patent Application**") and foreign counterparts as further described at Exhibit A, any continuations, continuations-in-part or divisionals or other Patents claiming priority to the Initial Patent Application or foreign counterparts thereto, and all Patents issuing from such Patents.

1.32 "**Virovek Technology**" means the invention disclosed in the Initial Patent Application.

ARTICLE 2

GRANT OF LICENSES

2.1 **License to Avalanche**. Subject to the terms and upon the conditions set forth in this Agreement, Virovek hereby grants, and Avalanche accepts, a royalty-bearing, non-exclusive, non-transferable, sublicensable license under the Virovek Patents and Virovek Know-How to develop, make, have made, use and Commercialize Licensed Products in the Field and in the Territory.

2.2 **Sublicensing**. Subject to the terms and upon the conditions of this Agreement, Avalanche shall have the right to grant Sublicenses to Third Parties, provided that such Sublicenses are consistent with the applicable terms of this Agreement. No Sublicense granted by Avalanche under this Section 2.2 shall relieve Avalanche of its obligations of performance under this Agreement.

2.3 **Right of Notice and First Negotiation**. In the event that Virovek enters into discussions or negotiations with respect to the terms under which Virovek may grant a license to any Third Party under the Virovek Patents and the Virovek Know-How (a "**Third Party License**"), Virovek will provide Avalanche with notice of such discussions or negotiations [*] Following receipt of such notice from Virovek, Avalanche shall have the first right to negotiate with Virovek terms and conditions for converting this license to an exclusive license [*] (an "**Exclusive License**"). If Avalanche desires to exercise such right, it shall so notify Virovek within [*] after receiving notice from Virovek. The Parties shall negotiate in good faith for a period of up

to [*] (the "**Negotiation Period**") after Avalanche receives notice of Virovek 's discussions or negotiations with a Third Party. During the Negotiation Period, Virovek will suspend further discussions or negotiations with any Third Party in relation to a Third Party License. The Parties may extend the Negotiation Period by mutual written agreement for a period of up to [*]. If the Parties fail to execute an Exclusive License at the end of the Negotiation Period, [*]

ARTICLE 3

CONSIDERATION

3.1 **License Issue Fee**. Avalanche shall pay to Virovek a license issue fee of [*], payable in two installments, in consideration for the rights granted to Avalanche under this Agreement:

(a) A one-time payment of [*] within [*]; and

(b) A one-time payment of [*] within [*]

The license issue fee is non-refundable and non-creditable against any milestone payments or royalties payable under this Agreement.

3.2 **Annual License Fee**. Avalanche shall pay to Virovek an annual fee of [*] (the "**Annual Fee"**) to maintain the rights granted to it herein. The Annual Fee shall be payable to Virovek's nominated bank account within [*] days of Avalanche's receipt of a valid invoice from Virovek for the amount of the Annual Fee, which invoice shall be issued by Virovek following each anniversary of the Effective Date, commencing with the first anniversary of the Effective Date.

3.3 **Royalty Payments**. In partial consideration for the license granted hereunder, and subject to the terms and conditions of this Agreement, subject to Section 3.9, Avalanche shall pay to Virovek during the Term a royalty (the " **Royalty**") on incremental annual Net Sales of Avalanche Products by Avalanche, its Affiliates and Sublicensees, as follows:

Portion of Annual Net Sales of Avalanche Products	**Royalty Percentage**
[*]	[*]
>[*] ≤ [*]	[*]
>[*] ≤ [*]	[*]
>[*]	[*]

By way of example, if Net Sales of Avalanche Products equals [*] in a calendar year, the royalty rate on the first [*] of Net Sales will be [*] and the royalty rate on the remaining [*] of Net Sales will be [*]

3.4 Royalty Term; Abatement.

(a) Avalanche's obligation to pay royalties with respect to each Avalanche Product pursuant to Section 3.3 in each country in the Territory shall apply and continue for so long as one or more Valid Claims of the Virovek Patents cover the manufacture, use or sale of such Avalanche Product in such country at the time when the Avalanche Product is manufactured, used or sold in such country.

(b) In the event that the total annual royalties (including the Royalty) that Avalanche is required to pay to Virovek and all other royalties payable by Avalanche, its Affiliates and Sublicensees to any Third Parties (together the "**Royalty Recipients**") in connection with the development, manufacture or Commercialization of a given Avalanche Product exceed [*] the royalties payable to each of the Royalty Recipients shall be reduced [*]

3.5 Royalty calculation and reporting. Royalty obligations under this Article 3 shall begin to accrue upon the first date upon which a Net Sale of an Avalanche Product occurs. All royalty payment obligations that have accrued on Net Sales made during a Calendar Quarter shall be due and payable to Virovek [*] after the end of the Calendar Quarter. Together with any payment of such royalties, Avalanche shall send to Virovek a written report setting forth the following in detail information necessary to confirm the calculation of Net Sales of Avalanche Products and the royalty payments payable during such Calendar Quarter. If no royalty shall be due, Avalanche shall so report.

3.6 Revenue Allocation. The Parties agree that any Third Party Revenue received by Avalanche from any Sublicensees will be shared between the Parties as follows:

(a) Third Party Revenue received with respect to Other Products that are Standard Products shall be apportioned [*] to Virovek, and [*]to Avalanche;

(b) Third Party Revenue received with respect to Other Products that are Improved Products shall be apportioned [*] Virovek, and [*] to Avalanche.

(c) Avalanche's payment obligations under this Section 3.6 shall apply and continue for so long as one or more Valid Claims of the Virovek Patents cover the manufacture, use or sale of such Other Product in such country at the time when the Other Product is manufactured, used or sold in such country.

3.7 Payment of Third Party Revenue. Avalanche shall account to Virovek and pay payments due to Virovek with respect to Third Party Revenue owed to Virovek pursuant to Section 3.6 [*] Avalanche will provide a statement specifying the total amount Avalanche received, the deductions from such revenues taken to calculate Third Party Revenue payments due pursuant to Section 3.6, and the net Third Party Revenue payable to Virovek. Avalanche shall pay all such amounts to Virovek's nominated bank account.

3.8 Payment Mechanics. All monies due to Virovek shall be paid in United States dollars. In the event that any Licensed Products shall be sold in a currency other than United States dollars, the Net Sales of Avalanche Products for the reporting period, or any other amounts upon

which payments are due to Virovek, shall be converted for the purpose of calculation of such royalty or amount into its equivalent dollar value [*] Any amounts not paid by Avalanche when due under this Agreement will be subject to interest from and including the date payment is due through and including the date upon which Virovek has collected the funds in accordance herewith [*] Virovek will pay any and all taxes levied on account of any payments made to it under this Agreement. If any taxes are paid or required to be withheld by Avalanche for the benefit of Virovek on account of any royalty or other payments to Virovek under this Agreement, Avalanche will (a) deduct such taxes from the amount of royalty or other payments otherwise due to Virovek, (b) timely pay the taxes to the proper taxing authority, and (c) send proof of payment to Virovek and certify its receipt by the taxing authority as promptly as practicable following such payment.

3.9 **Records**. Avalanche shall keep and maintain full, true and accurate books of account containing all particulars that may be necessary for the purpose of confirming the amounts payable to Virovek pursuant to this Agreement. The books of account shall be kept at Avalanche's principal place of business. The books of account and the supporting data shall be made available to an independent auditor reasonably acceptable to Virovek [*] starting in the year in which the Audit Trigger occurs, at reasonable times during normal business hours upon at least ten (10) days advance written notice. Such audit may be conducted as to Net Sales and payment-related records until the expiration of the [*] period following the end of the calendar year to which they pertain and shall be made available under this Section 3.9 for the sole purpose of verifying Avalanche's royalty statement or compliance in other respects with this Agreement. The costs and expenses relating to such inspection shall be borne by Virovek, except that if an audit reveals that Avalanche's royalties calculated for any quarter period were underpaid by more than [*], Avalanche shall bear the costs of such audit in full.

ARTICLE 4

DEVELOPMENT AND COMMERCIALIZATION

4.1 **Development and Commercialization**. Avalanche shall use commercially reasonable efforts to further develop and Commercialize for use in connection with Licensed Products in the Field the Virovek Technology, itself or with or through Third Party Sublicensees. Virovek shall use commercially reasonable efforts to cooperate with Avalanche's efforts to further develop and Commercialize for use in connection with Licensed Products in the Field the Virovek Technology.

ARTICLE 5

IP OWNERSHIP; PATENT PROSECUTION AND ENFORCEMENT

5.1 **Limitation**. Except as expressly set forth in this Agreement, neither Party is granted any license or other right with respect to intellectual property rights Controlled by the other Party.

5.2 **Ownership of Improvements**. The Parties agree that ownership of all inventions and all intellectual property rights therein, arising out of any use of the Virovek Technology conducted under this Agreement, including without limitation Improvements and other inventions

that are made by employees, independent contractors, or agents of either Party shall be governed by US laws of inventorship. In relation to any jointly created Improvements, each Party shall own an equal undivided interest in such Improvements, with no duty of accounting to the other Party (subject to the remainder of this Section 5.2). The Parties agree that any Virovek Improvements, and Virovek's ownership interest in any jointly created Improvements shall be included within the Virovek Patents or the Virovek Know-How and shall be subject to the terms of the licenses granted under this Agreement. For the avoidance of doubt, inventions developed solely by Avalanche shall belong to Avalanche, and inventions developed solely by Virovek shall belong to Virovek.

5.3 Patent Prosecution. Virovek shall have the first right, at its sole cost and expense, to conduct and control prosecution, maintenance, challenges against validity and unenforceability or patentability with respect to the Virovek Patents. At Virovek's reasonable request, Avalanche shall cooperate with and assist Virovek in connection with such activities. Virovek shall not abandon any of the Virovek Patents in the Territory without providing reasonable prior written notice to Avalanche of such intention to surrender and providing Avalanche an opportunity to assume responsibility for prosecution of such Licensed Patent, at its sole cost. If Avalanche elects to assume such responsibility, Virovek shall assign such Virovek Patent to Avalanche, and such Virovek Patent shall no longer be subject to this Agreement (and no claims of such Patent shall be eligible to be Valid Claims for purposes of Section 1.27).

5.4 Enforcement of Virovek Technology. If either Party should become aware of any actual or threatened infringement or misappropriation by a Third Party of any rights included in the Virovek Patents or Virovek Know-How (a "**Product Infringement**"), it shall promptly notify the other Party in writing, and provide any available information relating to such alleged Product Infringement. Avalanche shall have the first right, but not the obligation, to bring or control, at its own expense, any enforcement action relating to such Product Infringement, but shall keep Virovek informed in relation to all significant decisions. Virovek shall reasonably cooperate in any such enforcement and as necessary, join or be joined as a party to such action, provided that Avalanche agrees to reimburse Virovek for all of its out-of-pocket costs, damages and expenses, including reasonable attorneys' fees that Virovek may incur in relation to such assistance or joinder, including any award of costs against it in any judgment. If Avalanche elects not to bring a claim in relation to such Product Infringement, [*] Virovek shall then have the right, at its own expense, to enforce the Virovek Patents or Virovek Know-How. In the event that Virovek brings such an action, Avalanche shall reasonably cooperate in any such enforcement and as necessary, agree to join or be joined as a party to such action, provided that Virovek agrees to reimburse Avalanche for all of its out-of-pocket costs, damages and expenses, including reasonable attorneys' fees that Avalanche may incur in relation to such assistance or joinder, including any award of costs against it in any judgment. In each case, any costs, expenses or damages hereunder to be reimbursed by the Party bringing the enforcement action shall be paid by the owing Party to the other Party [*] or receipt of evidence in writing that the costs, damages and expenses have been incurred. Any amount recovered in an action or suit to enforce the Virovek Patents or Virovek Know-How shall be returned to the Party bringing such action, after the reimbursement of each Party's out-of-pocket costs, including reasonable attorneys' fees, except that if Avalanche is the Party bringing such action, such amount shall be treated as Net Sales of Avalanche Products by Avalanche for the purposes of Section 3.3.

5.5 **Infringement of Third Party Intellectual Property Rights**. If a Third Party brings a claim or allegation of infringement, by reason of the manufacture, use or sale of a Licensed Product in the Field and in the Territory, of such Third Party's Patent rights, the Party first receiving notice of such claim or allegation shall notify the other Party in writing and shall share information relating thereto with such other Party (if necessary, pursuant to a common interest agreement).

ARTICLE 6

CONFIDENTIALITY

6.1 **Use, Nondisclosure**. With respect to the Confidential Information of the other Party, each Party agrees, during the term of this Agreement and for [*] after this Agreement is terminated, or, in the case of Confidential Information that is a trade secret, until such Confidential Information is no longer a trade secret, as follows:

(a) Each Party shall hold the other Party's Confidential Information in confidence and take reasonable precautions to protect the same (including, without limitation, all precautions such Party employs with respect to its own confidential information).

(b) Each Party agrees not to divulge the other Party's Confidential Information to any Third Party unless approved in writing by the other Party, provided that in each case, such Third Party agrees to be bound by confidentiality provisions at least as restrictive as those contained in this Section 6;

(c) Each Party agrees not to make any use whatsoever at any time of the other Party's Confidential Information, except for the purpose of performing the Party's obligations under this Agreement;

(d) Each Party agrees not to use the other Party's Confidential Information as the basis for beginning any new research and development programs; and

(e) Each Party agrees not to copy or reverse engineer the other Party's Confidential Information.

6.2 At the conclusion of this Agreement, each Party shall [*] either return the other's Confidential Information in its possession (including all copies) or shall, at the disclosing Party's direction, destroy such Confidential Information (including all copies) and certify its destruction to the disclosing Party.

6.3 **Exclusions**. The term "Confidential Information" shall not include any information which: (a) is in the public domain at the time of disclosure or enters the public domain following disclosure through no fault of the receiving Party, (b) is already in the receiving Party's possession prior to disclosure hereunder (as reflected by such Party's written records) or is subsequently disclosed to the receiving Party with no obligation of confidentiality by a third Party having the right to disclose it, (c) is independently developed by the receiving Party without reference to the disclosing Party's Confidential Information, or (d) is required to be disclosed

pursuant to an order of any competent court or government agency or rules of a securities exchange with prior notice to disclosing Party, or as required by any Regulatory Authority, but shall notify the other Party prior to disclosing such information, and shall cooperate with the other Party using its commercially reasonable efforts either to enable the disclosing Party to seek protective measures for the Confidential Information, or to seek confidential treatment of such Confidential Information, and will use commercially reasonable efforts to limit any disclosure required to be made to any such agency to the minimum required for to meet the requirements of such order.

6.4 **Necessary disclosures:** Each Party may disclose the Confidential Information it receives under this Agreement to (i) its employees, contractors and permitted Sublicensees, (ii) to a potential or actual acquirer of such Party or the assets of such Party to which this Agreement relates, (iii) for the purposes of Patent filing, prosecution and enforcement and (iv) to its advisors, provided that in each of (i), (ii) and (iv), the disclosure is limited to the extent required for the performance of either Party's obligations under this Agreement, and provided that in each such case the individuals are subject to obligations of confidentiality in relation to such information no less stringent than those contained in this Agreement.

6.5 **Publicity**. The Parties agree that no publicity release or announcement concerning the transactions contemplated hereby will be issued without the advance written consent of the other Parties, such consent not to be unreasonably withheld, except as such release or announcement may be required (a) by applicable Laws, (b) for filings with governmental agencies, (c) for prosecuting or defending litigation, and (d) for complying with applicable governmental regulations, court orders, and legal requirements, including filings with the U.S. Securities Exchange Commission and with Regulatory Authorities, in each of which cases the Party required to make such release or announcement will, to the extent reasonably practicable before making any such release or announcement, afford the other Parties with a reasonable opportunity to review and comment upon such release or announcement and use reasonable efforts to seek confidential treatment of such information.

ARTICLE 7

ADDITIONAL COVENANTS AND AGREEMENTS OF THE PARTIES

7.1 **Technology Transfer**. As promptly as practicable but in any event no more than [*] after the Effective Date, Virovek shall make available to Avalanche any tangible copies of the Virovek Know-How in its Control (or copies thereof) that are necessary for Avalanche to exercise its rights under this Agreement.

7.2 **Compliance with Law**. Each Party will comply in all material respects with all applicable Laws in performing its obligations and exercising its rights under this Agreement.

ARTICLE 8

REPRESENTATIONS AND WARRANTIES

8.1 **By Both Parties**. Each Party represents and warrants the following:

[*] = 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.

(a) it is duly organized, validly existing, and in good standing under the laws of the state and/or nation of its organization;

(b) it has all requisite corporate power and authority to enter into this Agreement and perform its obligations hereunder and grant the rights it purports to grant hereunder, and it has taken all necessary corporate action on its part required to authorize the execution and delivery of the Agreement and the performance of its obligations hereunder;

(c) the Agreement has been duly executed and delivered on behalf of it, and constitutes a legal, valid, and binding obligation of such Party and is enforceable against it in accordance with its terms;

(d) the execution, delivery, and performance of this Agreement by it does not, and the consummation of the transactions contemplated hereby will not, violate or conflict with any provisions of its organizational documents, bylaws, any law or regulation applicable to it, or any agreement, instrument, order, judgment, or decree to which it is a Party or by which it is bound that would materially affect its ability to consummate the transaction contemplated hereby or impair the rights being granted to the other Party; and

(e) all necessary consents, approvals, and authorizations of all governmental authorities and other Third Parties required to be obtained by such Party in connection with the entry into this Agreement have been obtained.

8.2 IMPLIED WARRANTIES. EXCEPT AS EXPRESSLY PROVIDED IN THIS ARTICLE 8, NEITHER PARTY MAKES ANY REPRESENTATIONS OR WARRANTIES AS TO THE VIROVEK PATENTS OR VIROVEK KNOW-HOW OR ANY OTHER MATTER, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY AND ALL IMPLIED OR STATUTORY WARRANTIES, INCLUDING, WITHOUT LIMITATION, ALL IMPLIED WARRANTIES OF TITLE, NON-INFRINGEMENT, MERCHANTABILITY, AND FITNESS FOR A PARTICULAR PURPOSE. NOTHING IN THIS AGREEMENT SHALL BE CONSTRUED AS A WARRANTY OR REPRESENTATION BY VIROVEK AS TO THE VALIDITY OR SCOPE OF ANY OF THE VIROVEK PATENTS.

ARTICLE 9

INDEMNIFICATION

9.1 Indemnity by Avalanche. Avalanche shall indemnify Virovek and its directors, officers, employees and agents from any costs, damages, liabilities or expenses (including reasonable legal fees and expenses) in connection with claims or actions brought by Third Parties (collectively, "**Losses"**) to the extent arising from the breach by or on behalf of Avalanche of its representations, warranties or obligations hereunder, or the negligence or willful misconduct of Avalanche, its Affiliates, independent contractors or Sublicensees.

9.2 Indemnity by Virovek. Virovek shall indemnify Avalanche and its directors, officers, employees and agents from any Losses to the extent arising from the breach by or on

behalf of Virovek of its representations, warranties or obligations hereunder, or the negligence or willful misconduct of Virovek, its Affiliates or independent contractors.

9.3 Conditions of Indemnification. The Indemnifying Party's indemnity obligations as provided for in this Article 9 shall be conditioned upon the following:

(a) the Indemnified Party providing prompt written notice of the applicable Claim to the Indemnifying Party;

(b) the Indemnified Party permitting the Indemnifying Party to have sole control over the investigation, defense, or settlement of the applicable Claim;

(c) the Indemnified Party reasonably cooperating with the Indemnifying Party in the investigation and defense of such Claim; and

(d) the Indemnified Party's agreement not to compromise or otherwise settle any such Claim without the Indemnifying Party's prior written consent, which consent shall not be unreasonably withheld or delayed.

9.4 Insurance. Each Party shall maintain insurance in the amounts of [*].

9.5 Limitation of Liability. NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, OR INDIRECT DAMAGES ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES. NOTWITHSTANDING THE FOREGOING, NOTHING IN THIS SECTION 9.4 IS INTENDED TO LIMIT OR RESTRICT THE INDEMNIFICATION RIGHTS OR OBLIGATIONS OF ANY PARTY UNDER ARTICLE 9, OR DAMAGES AVAILABLE FOR A BREACH OF CONFIDENTIALITY OBLIGATIONS IN ARTICLE 6.

ARTICLE 10

TERM AND TERMINATION

10.1 Term. This Agreement shall be effective as of the Effective Date and, unless earlier terminated by mutual agreement or in accordance with other provisions herein, shall remain in effect until the expiration or abandonment of the last of the Virovek Patents included in the Virovek Technology.

10.2 Termination. Anything herein to the contrary notwithstanding, this Agreement may be terminated as follows:

(a) Avalanche Voluntary Termination. Avalanche may terminate this Agreement at any time by giving [*] written notice to Virovek.

(b) Termination For Default. Each Party shall have the right to terminate this Agreement for default due to the other Party's uncured failure to comply in any material respect with the terms and conditions of this Agreement. At least [*] (or, in the case of Avalanche's

failure to make any payment hereunder when due, [*]) prior to any such termination for default, the Party seeking to so terminate shall give the other Party written notice of its intention to terminate this Agreement in accordance with the provisions of this Section 10.2(b), which notice shall set forth the default(s) which form the basis for such termination. If the defaulting Party fails to correct such default(s) by the end of the applicable notice period, the other Party immediately may terminate this Agreement.

10.3 Consequences of Expiration or Termination.

(a) In the event of expiration or any termination of this Agreement, all rights and obligations of the Parties under this Agreement shall terminate, except as set forth in this Section 10.3.

(b) In the event of any termination (but not expiration) of this Agreement:

(i) All rights to the Virovek Technology and any Virovek Improvements shall revert to Virovek;

(ii) Avalanche shall immediately cease any use and/or exploitation of the Virovek Patents and Virovek Know-How and cease developing, using, manufacturing, selling, distributing and/or licensing any Licensed Product, either directly or indirectly, and shall cause its Affiliates, and require its Sublicensees, to do the same; and

(iii) Each Party shall, at its election, either deliver to the other Party or destroy, and shall cause its agents, consultants and Sublicensees to deliver to the other Party or destroy, all embodiments of the other Party's Confidential Information or any part thereof in their possession, power or control; *provided, however,* that such Party may retain, and permit its Sublicensees to retain, one archival copy of such Confidential Information solely for purposes of monitoring its compliance with Article 6 hereof.

(c) Neither expiration of this Agreement, nor termination of this Agreement for any reason, shall relieve the Parties of any obligation accruing prior thereto and shall be without prejudice to the rights and remedies of either Party with respect to any antecedent breach of the provisions of this Agreement. Without limiting the generality of the foregoing, no expiration or termination of this Agreement, whether by lapse of time or otherwise, shall serve to terminate the obligations of the Parties hereto under Sections 8.3, 10.1 and 10.3, and Articles 1, 6, 9 (but as to Sections 9.1 through 9.4 solely as to claims arising from activities during the term of this Agreement) and 11 and such other Sections as by their nature should survive, and such obligations shall survive any such expiration or termination.

ARTICLE 11

MISCELLANEOUS

11.1 Assignment. Neither Party may assign this Agreement without prior written consent from the other Party, except that no such consent shall be required for either Party to assign its rights or transfer its obligations to its Affiliates or in connection with the sale or transfer of the

[*] = 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.

majority of its stock or all or substantially all of its assets to which this Agreement relates, whether as part of a merger, acquisition, or asset sale. Any assignment in violation of this Agreement will be null and void. This Agreement benefits and binds the parties and their respective successors and permitted assigns.

11.2 **Severability**. If any provision or provisions of this Agreement shall, to any extent, be held to be invalid or unenforceable by a court of competent jurisdiction, the remainder of this Agreement shall not be affected thereby and shall be valid and enforceable to the fullest extent permitted by law. However, in case such invalidation or unenforceability injures the rights and interests of a Party, the Parties hereto shall renegotiate this Agreement in good faith to replace any invalid or unenforceable provision with a valid and enforceable one such that the objectives contemplated by the Parties when entering this Agreement may be realized.

11.3 **Entirety of Agreement; Modification**. This Agreement, together with all exhibits hereto, constitute the entire, final, and complete agreement and understanding between the Parties, and replace and supersede all prior discussions and agreements between them with respect to the subject matter hereof, [*] No modification or amendment to this Agreement shall be valid or binding upon the Parties hereto unless made in writing and duly executed on behalf of each of the Parties hereto.

11.4 **Governing Law**. This Agreement shall be governed by and interpreted in accordance with the laws of the State of California without giving effect to any choice of law principles that would require the application of the laws of a different state or country.

11.5 **Force Majeure**. If a Party is prevented from complying, either totally or in part, with any of the terms or provisions set forth herein by reason of force majeure, including, by way of example and not of limitation, fire, flood, explosion, storm, earthquake, strike, lockout or other labor dispute, riot, war, rebellion, terrorist act, accidents, acts of God, failure of suppliers or any other similar cause, in each case to the extent beyond its reasonable control, said Party will promptly provide written notice of same to the other Parties. Such notice will identify the requirements of this Agreement or such of its obligations as may be affected, and such obligations will be suspended during the period of such disability, provided that the Party prevented from performing hereunder will use reasonable efforts to remove such disability and will continue performance whenever such causes are removed. The Party so affected will give to the other Party a good faith estimate of the continuing effect of the force majeure condition and the duration of the affected Party's nonperformance.

11.6 **Notice**. Any notice required to be given by a Party in connection with this Agreement shall be given in the English language by prepaid airmail, express delivery service, or facsimile, and shall be deemed to have been given for all purposes (a) when received, if sent by express delivery service, (b) three (3) business days after mailing, if mailed by airmail, or (c) when received by recipient, if sent by facsimile transmission with electronic confirmation of transmission if transmission is confirmed during the recipient's normal business hours, or otherwise on the recipient's next business day. Unless otherwise specified in writing, the Parties' addresses for notice purposes are as follows:

To Virovek:	3521 Investment Boulevard, Suite 1 Hayward, CA 94545 Attn: [*]
With a copy to (which shall not constitute notice):	[*]
To Avalanche:	665 Third Street, Suite 250 San Francisco, CA 94107 Attn: [*]
With a copy to (which shall not constitute notice):	[*]

11.7 Dispute Resolution. If any dispute arises relating to this Agreement, prior to instituting any termination under Sections 10.2(b) or any lawsuit or other dispute resolution process on account of such dispute, the Parties will attempt in good faith to settle such dispute first by negotiation and consultation between themselves, including referral of such dispute to the CEOs of the Parties. If the CEOs are unable to resolve such dispute or agree upon a mechanism to resolve such dispute [*] after such matter is first submitted to them for resolution, then either Party may then submit such issue for resolution by a court of competent jurisdiction in California.

11.8 Construction. The Parties have participated jointly in the negotiation and drafting of this Agreement. In the event that an ambiguity or question of intent or interpretation arises, this Agreement shall be construed as if drafted jointly by the Parties and no presumption or burden of proof shall arise favoring or disfavoring any Party by virtue of the authorship of any of the provisions of this Agreement. Except where the context otherwise requires, where used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders and the word "or" is used in the inclusive sense (and/or). The captions of this Agreement are for convenience of reference only and in no way define, describe, extend or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The term "includes" and "including" as used herein means including, but not limited to.

11.9 Use of Names. Neither Party will use the name or trademark of the other Party in relation to this Agreement in any advertising, press release or other form of publicity without the prior written consent of the other Party, such consent not to be unreasonably withheld. This restriction shall not apply to materials used by either Party solely for financing purposes or to documents available to the public that identify the existence of the Agreement.

11.10 Counterparts; Facsimiles. This Agreement may be executed in one or more counterparts, each of which shall be an original and all of which shall constitute together the same document. For purposes of this Agreement and any other document required to be delivered pursuant to this Agreement, facsimiles or electronic copies of signatures shall be deemed to be original signatures. In addition, if any of the Parties sign facsimile copies of this Agreement, such copies shall be deemed originals.

11.11 Waiver. Any delay in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights

to the future enforcement of its rights under this Agreement unless such Party provides an express written and signed waiver as to a particular matter for a particular period of time.

[Remainder of page intentionally left blank]

[*] = 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.

In Witness Whereof, the Parties have caused this Agreement to be executed by their duly authorized officers as of the Effective Date.

Virovek, Inc.

By:

Name:

Title:

Date:

Avalanche Biotechnologies, Inc.

By:

Name:

Title:

Date:

[*] = 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 A

Virovek Patents

Patent Filing	Type	Territory	Filing Date
[*]	[*]	[*]	[*]

[*] = 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 10.48

October 24, 2018

Leone Patterson
337 Channing Way
Alameda, California 94502

Re: Amended and Restated Employment Terms

Dear Leone:

This letter agreement (the "Agreement") sets forth the amended and restated terms of your employment with Adverum Biotechnologies, Inc. (the "Company"). These terms became effective on October 18, 2018, and shall supersede and replace the terms set forth in your earlier offer letter from the Company dated May 31, 2016.

1. Role

You will serve as the President and Chief Executive Officer of the Company, reporting to the Board of Directors (the "Board"). During the period in which you are employed as the Company's President and Chief Executive Officer, you will serve as a member of the Board, subject to any required Board and/or stockholder approval. Unless the Board provides otherwise, upon your termination of employment as the Company's President and Chief Executive Officer for any reason, you will automatically and without further action immediately be deemed to have resigned from the Board.

2. Compensation and Benefits.

Your current compensation is equal to an annual base salary of $371,300 ("Current Salary"), plus retention bonuses at the rate of $300,000 per year, payable in equal quarterly installments at the beginning of each quarter. Effective as of January 1, 2019, your base salary will be increased to $515,000 annually (the "New Salary"), and the quarterly retention bonuses will cease. (For sake of clarity, you will not receive a retention bonus for the first quarter of 2019.) Your salary will be paid in accordance with the Company's standard payroll schedule, subject to standard payroll deductions and withholdings.

You will remain eligible for a 2018 bonus, with the target of such bonus to be equal to 40% of the Current Salary for the period of 2018 that you served as Chief Financial Officer (1/3 of the year), and 55% of $671,300 (the sum of Current Salary and total annual retention bonuses) for the remainder of 2018 (2/3 of the year). For example, if you earn a bonus for 2018 at 100% of target, it would be for 40%*$371,300*1/3 + 55%*$671,300*2/3, or $295,650. Your target bonus for 2019 will be equal to 55% of the New Salary (or such higher amount if your salary is increased in the future). Annual bonuses are earned when paid, and thus you must be actively employed through and including the date the bonus is paid in order to earn the bonus. Your annual bonus

will be calculated based on attainment of individual goals (including corporate and personal objectives) to be determined in the sole discretion of the Board each year. Bonus payments will be in the form of cash, and will be subject to applicable payroll deductions and all required withholdings.

You will continue to be eligible to participate in the Company's general employee benefits in accordance with the terms, conditions and limitations of any such benefit plans, as in effect from time to time.

3. Stock Option and Restricted Stock Unit grants.

As of the date of this Agreement, you have been granted certain options and restricted stock units, including an option to purchase 150,000 shares of the Company's common stock that was granted on October 18, 2018 in connection with your promotion to President and Chief Executive Officer. Those options and previously granted options and restricted stock units will continue to be governed in all respects by the terms of the applicable equity incentive plan and option or restricted stock unit agreements.

4. Confidentiality and Proprietary Information Obligations.

(a) **Company Policies and Proprietary Information Agreement**. You will be required to remain in compliance with the terms of the Employee Proprietary Information and Invention Assignment Agreement that you previously executed, as well as the Company's standard policies and procedures.

(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 Board. 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) 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.

5. 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 that 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.

6. At Will Employment; Amended and Restated Change in Control and Severance Agreement.

You will be eligible for severance benefits under the terms of the Amended and Restated Change in Control and Severance Agreement attached hereto as Exhibit A.

Your employment relationship with the Company remains "at-will." 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. The Company also has the right to reassign you or change your compensation at any time, with or without cause or 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 member of the Board.

7. Miscellaneous.

7.1 Entire Agreement. This Agreement, together with any agreements referenced herein, 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 (including, without limitation, your previous offer letter from the Company dated May 31, 2016).

7.2 Succession and Assignment. This Agreement is personal to you and shall not be assigned by you. Any purported assignment by you shall be null and void from the initial date of the purported assignment. The Company may assign this Agreement to any successor or assign (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Company. This Agreement shall inure to the benefit of the Company and permitted successors and assigns.

7.3 Enforceability. 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.

7.4 Governing law and Jurisdiction. 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 action or proceeding by either of the parties to enforce this Agreement shall be brought only in a state or federal court located in the state of California, county of San Mateo. The parties hereby irrevocably submit to the exclusive jurisdiction of such courts and waive the defense of inconvenient forum to the maintenance of any such action or proceeding in such venue.

7.5 Headings and Captions. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

7.6 **No Construction against Drafter**. Any ambiguity in this Agreement shall not be construed against either party as the drafter.

7.7 **Waiver**. 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.

7.8 **Counterparts**. 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.

8. Acknowledgement of Full Understanding. YOU ACKNOWLEDGE AND AGREE THAT YOU HAVE FULLY READ, UNDERSTAND AND VOLUNTARILY ENTER INTO THIS AGREEMENT. YOU ACKNOWLEDGE AND AGREE THAT YOU HAVE HAD AN OPPORTUNITY TO ASK QUESTIONS AND CONSULT WITH AN ATTORNEY OF YOUR CHOICE BEFORE SIGNING THIS AGREEMENT.

Please sign and date this letter and return it to me to confirm your continued employment on the terms as set forth above.

Sincerely,
Adverum Biotechnologies, Inc.

/s/ Paul Cleveland
Paul B. Cleveland, Chair of the Board of Directors

Understood and Accepted:

/s/ Leone Patterson
Leone Patterson

Date: October 24, 2018

EXHIBIT A TO LETTER AGREEMENT

AMENDED AND RESTATED CHANGE IN CONTROL AND SEVERANCE AGREEMENT

EXHIBIT 10.49

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 Leone Patterson ("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 (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 twelve (12) 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 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 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) eighteen (18) months of Executive's Base Salary at the rate in effect immediately before the date of the Covered Termination and (ii) Executive's 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) eighteen (18) months following 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) the Executive's commission or the attempted commission of or participation in any crime involving fraud, dishonesty or moral turpitude that results in (or might have reasonably resulted in) material harm to the business of the Company; (ii) intentional and material damage to the Company's property and/or misappropriation of Company funds; (iii) conduct that constitutes gross insubordination, incompetence or habitual neglect of duties that results in (or might have reasonably resulted in) material harm to the business of the Company that has not been cured within 30 days after written notice from the Executive's immediate supervisor or in the case of the chief executive officer, from the Board; 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; (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. 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) Interference with Business. Consistent with 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, directly or indirectly solicit, induce, recruit or encourage any officer, director, employee, independent contractor or consultant of the Company who was employed by or affiliated with the Company at the time of termination to leave the Company or terminate his or her employment or relationship with the Company. Executive agrees not to make, publish or communicate at any time to any person or entity or in any public forum any defamatory or disparaging remarks, comments or statements concerning the Company or its businesses, or any of its employees, officers, and existing and prospective customers, suppliers, investors and other associated third parties. Executive agrees not to use the Company's Proprietary Information (as defined in Executive's Proprietary Information Agreement) to directly or indirectly interrupt, disturb or interfere with the Company's relationships with any customer, vendor, supplier, licensor, investor, consultant, independent contractor or other business partner, or to compete unfairly with 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. Miscellaneous Provisions.

(a) Section 409A.

(i) General. The payments and benefits under this Agreement are intended to qualify for exemptions from the application of Section 409A of the Code, and this Agreement will be construed to the greatest extent possible as consistent with those provisions, and to the extent not so exempt, this Agreement (and any definitions hereunder) will be construed in a manner that complies with Section 409A of the Code to the extent necessary to avoid adverse taxation under Section 409A of the Code.

(ii) 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 11(a)(iii) 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.

(iii) 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 11(a)(iii) shall be paid in a lump sum to Executive, and any remaining payments due under this Agreement shall be paid as otherwise provided herein.

(iv) Installment Payments. Each installment payment payable under this Agreement will be treated as a separate payment for purposes of Section 409A of the Code.

(v) 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 but not limited to the Change in Control and Severance Agreement between the parties hereto, dated as of June 10, 2016, as amended as of January 29, 2018.

(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:/s/ Paul Cleveland
Paul Cleveland, Chair of the Board of Directors

Date: October 24, 2018

EXECUTIVE

/s/ Leone Patterson
Leone Patterson

Date: October 24, 2018

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 No. 333-220894, No. 333-218465, No. 333-211439, No. 333-203398, No. 333-199296 on Form S-8 of our report dated March 6, 2018, relating to the 2017 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, 2018.

/s/ Deloitte & Touche LLP

San Jose, California
March 6, 2019

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

(1) Registration Statements on Form S-8 No. 333-223894, No. 333-218465, No. 333-211439, No. 333-203398, and No. 333-199296
(2) Registration Statement on Form S-3 No. 333-219890

of our report dated March 6, 2019, with respect to the consolidated financial statements of Adverum Biotechnologies Inc. included in this Annual Report (Form 10-K) of Adverum Biotechnologies Inc. for the year ended December 31, 2018.

/s/ Ernst & Young LLP

San Jose, California
March 6, 2019

Exhibit 31.1

CERTIFICATION OF THE PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF
THE SARBANES-OXLEY ACT OF 2002

I, Leone Patterson, 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, 2019

By: /s/ Leone Patterson
Name: Leone Patterson
Title: 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, 2019

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, 2018 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Leone Patterson, as Chief Executive Officer and 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, 2019

By: /s/ Leone Patterson
Leone Patterson
Chief Executive Officer, Chief Financial Officer
(Principal Executive and Financial Officer)