2021 ANNUAL REPORT

Included in the 2021 Annual Report:
Form 10-K (without exhibits) filed with the U.S. Securities and Exchange Commission on March 2, 2022

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2021

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 No. 001-37590

AVALO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	45-0705648
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

540 Gaither Road, Suite 400
Rockville, Maryland 20850
(Address of principal executive offices)
Telephone: (410) 522-8707
(Registrant's telephone number, including area code)
Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 Par Value	AVTX	Nasdaq Capital Market

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

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule12b-2 of the Exchange Act.

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

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

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

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

The aggregate market value of the registrant's shares of common stock held by non-affiliates of the registrant as of June 30, 2021 (which is the last business day of the registrant's most recently completed second fiscal quarter) based upon the closing market price of such stock on the Nasdaq Capital Market on that date was approximately $183.5 million. Shares of common stock held by each officer and directors and by each person known to be the registrant who owned 10% or more of the outstanding common stock have been excluded in that such person may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 28, 2022, there were 112,794,203 outstanding shares of the registrant's common stock, par value $0.001 per share.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A within 120 days after the end of the fiscal year ended December 31, 2021. Portions of such proxy statement are incorporated by reference into Part III of this Form 10-K.

TABLE OF CONTENTS

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This report and the information incorporated herein by reference contain forward-looking statements that involve a number of risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as "projects," "may," "might," "will," "could," "would," "should," "continue," "seeks," "aims," "predicts," "believes," "expects," "anticipates," "estimates," "intends," "plans," "potential," "pro forma" or other similar words (including their use in the negative), or by discussions of future matters such as: the future financial and operational outlook; the development of product candidates; and other statements that are not historical. These statements include but are not limited to statements under the captions "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" as well as other sections in this report. You should be aware that the occurrence of any of the events discussed under the caption "Risk Factors" and elsewhere in this report could substantially harm our business, results of operations and financial condition and cause our results to differ materially from those expressed or implied by our forward-looking statements. If any of these events occurs, the trading price of our common stock could decline and you could lose all or a part of the value of your shares of our common stock.

The cautionary statements made in this report are intended to be applicable to all related forward-looking statements wherever they may appear in this report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. 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.

As used in this report, the terms "Avalo," "Company," "we," "us," and "our" mean Avalo Therapeutics, Inc. and its subsidiaries unless the context indicates otherwise.

SUMMARY OF PRINCIPAL RISK FACTORS

This summary briefly states the principal risks and uncertainties facing our business that could affect our common stock, which are only a select portion of those risks. A more complete statement of those risks and uncertainties is set forth under Part I, Item 1A "Risk Factors" of this annual report. This summary is qualified in its entirety by that more complete statement. You should carefully read the entire "Risk Factors" section when considering the risks and uncertainties as part of your evaluation of our business.

- We will need substantial additional capital for the continued development of our product candidates and for our long-term operations, which might not be available to us on acceptable terms, or at all. Failure to obtain any necessary capital will force us to delay, limit or terminate our product development efforts or cease our operations.

- Servicing our debt requires a significant amount of cash, and we might not have or be able to obtain sufficient cash to pay our substantial debt.

- Under our Loan Agreement, our Lenders have broad discretion as to what qualifies as a Material Adverse Change that could cause the loan amounts due to be accelerated, thus exposing us to illiquidity. The limitations under our Loan Agreement may also restrict our operations or produce other adverse results.

- Armistice Capital Master Fund Ltd., (an affiliate of Armistice Capital, LLC and collectively "Armistice") has significant influence over us, and its interests may be different from or conflict with those of our other stockholders.

- Our product candidates that we intend to commercialize are in early stages of development. If we do not successfully complete preclinical testing and clinical development of our product candidates or experience significant delays in doing so, our business may be materially harmed.

- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

- Even if we complete the necessary clinical trials, we cannot predict when or if we will obtain marketing approval to commercialize a product candidate or the approval may be for a narrower indication than we expect.

- The marketing approval processes of the United States Food and Drug Administration (the "FDA") and comparable foreign regulatory authorities are lengthy, time-consuming, costly and inherently unpredictable. Our inability to obtain regulatory approval for our product candidates would substantially harm our business.

- We rely on third parties to conduct, supervise and monitor our clinical trials. The failure of these third parties to successfully carry out their contractual duties or meet expected deadlines could substantially harm our business because we might not obtain marketing approval for or commercialize our product candidates in a timely manner or at all.

- We use third parties to manufacture all of our product candidates. This may increase the risk that we will not have sufficient quantities of our product candidates to conduct our clinical trials or such quantities at an acceptable cost, which could result in the delay, prevention, or impairment of clinical development and commercialization of our product candidates.

- The ongoing COVID-19 pandemic has had an impact on our business operations and clinical trials and could continue, directly or indirectly, to adversely affect our business, results of operations and financial condition and our stock price.

- We might not be successful in our efforts to develop and commercialize our product candidates.

- Even if we were to obtain approval for our product candidates with the Rare Pediatric Disease Designation, the Rare Pediatric Disease Priority Review Voucher Program may no longer be in effect at the time of such approval or we might not be able to capture the value of the Rare Pediatric Disease Priority Review Voucher Program.

- If we are unable to obtain or maintain intellectual property rights, or if the scope of patent protection is not sufficiently broad, competitors could develop and commercialize products similar or identical to ours, and we might not be able to compete effectively in our market.

- If we breach the license and development agreements related to our product candidates, we could lose the ability to develop and commercialize our product candidates.

- We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

- If we fail to attract and keep management and other key personnel, as well as our board members, we may be unable to develop our product candidates or otherwise implement our business plan.

- If we are not able to comply with the applicable continued listing requirements or standards of The Nasdaq Stock Market, Nasdaq could delist our common stock.

- The market price of our stock is volatile, and you could lose all or part of your investment.

- Our Chief Executive Officer has interests in the development of AVTX-006 pursuant to a royalty agreement that may conflict with interests of stockholders.

- We have incurred significant net losses in most periods since our inception and we expect to continue to incur net losses in the future.

PART I

Item 1. Business.

Overview

Avalo Therapeutics, Inc. (the "Company", "Avalo" or "we") is a leading clinical-stage precision medicine company that discovers, develops, and commercializes targeted therapeutics for patients with significant unmet clinical need in immunology and rare genetic diseases. The Company has built a diverse portfolio of innovative therapies to deliver meaningful medical impact for patients in urgent need. Avalo's clinical candidates commonly have a proven mechanistic rationale, biomarkers and/or an established proof-of-concept to expedite and increase the probability of success.

Avalo was incorporated in Delaware, commenced operation in 2011 and completed its initial public offering in October 2015. In August 2021, the Company changed its corporate name from Cerecor Inc. to Avalo Therapeutics, Inc. and merged certain wholly-owned subsidiaries into the Company to consolidate its corporate structure. The name change underscores the Company's transition to developing innovative targeted therapies in immunology and rare genetic diseases.

Our Strategy

Our strategy for increasing stockholder value includes:

- Advancing our pipeline of compounds through development and to regulatory approval;
- Acquiring or licensing rights to targeted, complementary differentiated preclinical and clinical stage compounds;
- Developing the go-to-market strategy to quickly and effectively market, launch, and distribute each of our compounds that receive regulatory approval; and
- Opportunistically out-licensing rights to indications or geographies.

Pipeline Assets— Overview, Competition and Intellectual Property

Clinical-Stage Pipeline

The following chart summarizes key information about our clinical-stage pipeline and is followed by further detail for each program, including an overview, competition, licenses (if applicable), and market, data, and patent exclusivity/intellectual property:

Program	Mechanism of Action	Lead Indication	Designation	Clinical Development Stage			Anticipated Milestone
				Phase 1	Phase 2	Phase 3/Pivotal	
Immunology							
AVTX-002	Anti-LIGHT mAb	NEA	–				Phase 2 Top-line Data 4Q 2022
		Inflammatory bowel disease	–				*
		COVID-19 ARDS	Fast Track				**
AVTX-007	Anti-IL-18 mAb	Still's disease	–				Top-line Data 2023‡
Rare Genetic Diseases							
AVTX-801	D-Galactose replacement	PGM1-CDG	ODD RPDD Fast Track				Pivotal Trial Data 2023‡‡
AVTX-803	L-Fucose replacement	LAD II (SLC35C1-CDG)					Pivotal Trial Data 4Q 2022

* The Company is considering a possible randomized, double-blind, placebo-controlled clinical trial in moderate to severe refractory patients with IBD

** Further development of AVTX-002 for treatment of COVID-19 ARDS is currently dependent on third party funding

‡ Management is currently reviewing preliminary data and path forward related to this indication; updates will be forthcoming upon finalization of the review

‡‡ This study is sponsored by a third party; currently working with study sponsor to refine milestone timing

ARDS, acute respiratory distress syndrome; CDG, congenital disorder of glycosylation; IL, interleukin; LAD, leukocyte adhesion deficiency; mAb, monoclonal antibody; NEA, non-eosinophilic asthma; ODD, orphan drug designation; PGM1, phosphoglucomutase 1; RPDD, rare pediatric disease designation

AVTX-002: ***Anti-LIGHT monoclonal antibody for treatment of Non-Eosinophilic Asthma, moderate to severe Inflammatory Bowel Disease, and COVID-19 Acute Respiratory Distress Syndromes***

Overview: AVTX-002 is a fully human anti-LIGHT (**L**ymphotoxin-like, exhibits **I**nducible expression, and competes with HSV **G**lycoprotein D for **H**VEM, a receptor expressed by **T** lymphocytes) monoclonal antibody ("mAb"). It is also known as tumor necrosis factor superfamily member 14 ("TNFSF14"). To our knowledge, AVTX-002 is the only anti-LIGHT mAb in clinical development in the United States. It has the potential to treat a number of LIGHT-associated immune diseases. The Company is currently developing AVTX-002 for the treatment of non-eosinophilic asthma ("NEA"), inflammatory bowel disease ("IBD"), including moderate to severe Crohn's disease ("CD") and moderate to severe ulcerative colitis ("UC"), and COVID-19 acute respiratory distress syndrome ("ARDS") (with the potential expansion to a larger patient population in broader ARDS).

About Non-Eosinophilic Asthma: NEA is a significant subtype of asthma that encompasses approximately half of asthma patients. It is characterized by airway inflammation with the absence of eosinophils. NEA is associated with environmental and/ or host factors such as smoking cigarettes, pollution, infections and obesity. Patients present with respiratory symptoms such as wheeze, shortness of breath, cough and chest tightness.

About Inflammatory Bowel Disease: IBD is the broad term indicating chronic inflammation of the GI tract and includes both CD and UC.

- **Crohn's Disease:** Crohn's disease is an inflammatory bowel disease characterized by severe, chronic inflammation of the intestinal wall or any portion of the gastrointestinal tract. In Crohn's disease, the immune system responds to a stimulus, often an infection, but the response is abnormal. The immune system mistakenly targets the gastrointestinal system. This sustained and abnormal immune system activity causes chronic inflammation and irritation of the tissues of the gastrointestinal tract, resulting in the signs and symptoms of Crohn's disease.
- **About Ulcerative Colitis:** Ulcerative colitis is also an inflammatory bowel disease characterized by chronic inflammation and superficial ulcerations limited to the colon. Patients with the disease have bloody diarrhea, abdominal cramps and pain. With chronic disease, there is a risk of colon cancer.

About COVID-19 ARDS: ARDS is a severe inflammatory disease of the lungs caused by a buildup of excess fluid in the alveoli of the lungs. ARDS is a condition most commonly associated with illnesses such as sepsis, trauma, and viral and bacterial pneumonia. Current literature suggests that COVID-19 usually begins as an upper respiratory tract infection; however, for some patients, the COVID-19 virus enters the lower respiratory tract and causes direct injury to the lungs by filling the alveoli with excess fluid. Often times, as decrease in oxygenation occurs in the blood, breathing becomes distressed and organs become oxygen-deficient. The lungs attempt to heal, but the resulting inflammatory response often ends up damaging the lungs further. When a patient presents with symptoms associated with ARDS—shortness of breath, chest pain, rapid heart rate and reduced blood oxygen levels—they may be transported to the intensive care unit to be monitored and possibly treated with artificial or mechanical ventilation.

Competition:

- **NEA:** As of the date of this report, there are no FDA approved therapies specifically for NEA; however, Tezspire® (thymic stromal lymphopoietin blocker) was approved in December 2021 for the treatment of severe asthma in a broad population with no phenotype of biomarker limitations.

- **IBD:**
  - **CD:** There are numerous options available for the treatment of patients with moderate to severe Crohn's disease, including biologics and non-biologics. Products approved to treat this population include Remicade®, Humira®, Cimzia® (anti-TNFs), Stelara® (anti-IL 12 & IL 23), and Entyvio® (integrin receptor antagonist).
  - **UC:** There are currently a number of options available for the treatment of patients with moderate to severe Ulcerative Colitis. These products are similar to what is used to treat CD, however there are some different agents; products approved to treat this population include Remicade®, Humira® and Simponi® (anti-TNFs), Stelara® (anti-IL 12 & IL 23), Entyvio® (integrin receptor antagonist), Zeposia® (sphingosine 1-phosphate receptor modulator) and Xeljanz® (JAK inhibitor).

- **COVID-19 ARDS:** While there are multiple vaccines approved for COVID-19 (COMIRNATY, Spikevax, and Janssen Covid-19 vaccine), antiviral treatments (VEKLRY®, Paxlovid™ and Molnupiravir) and monoclonal antibody therapies under EUA (Evusheld®, REGEN-COV®, sotrovimab, bebtelovimab and bamlanivimab/etesevimab) which have varying efficacy dependent on the COVID-19 variant, there are only two products in the US authorized by the FDA under Emergency Use Authorization ("EUA") (ACTEMRA®, anti-IL-6 and Olumiant® a JAK inhibitor) to treat patients who are hospitalized and who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation. In the European Union, ACTEMRA/RoACTEMRA was also approved for use in COVID-19 patients. KINERET® (IL-1R antagonist/IL-1Ra) received European Medicines Agency ("EMA") approval for the use in COVID-19 in adult patients with pneumonia requiring supplemental oxygen (low or high flow oxygen) and who are at risk of developing severe respiratory failure, however, it is not approved under EUA for use in the United States.

License: On March 25, 2021, the Company entered into a license agreement with Kyowa Kirin Co., Ltd. ("KKC") for exclusive worldwide rights to develop, manufacture and commercialize AVTX-002 for all indications (the "KKC License Agreement"). The KKC License Agreement replaced the Amended and Restated Clinical Development and Option Agreement between the Company and KKC dated May 28, 2020.

Under the KKC License Agreement, the Company paid KKC an upfront license fee equal to $10 million. The Company is also required to pay KKC up to an aggregate of $112.5 million based on the achievement of specified development and regulatory milestones. Upon commercialization, the Company is required to pay KKC sales-based milestones aggregating up to $75 million tied to the achievement of annual net sales targets.

Additionally, the Company is required to pay KKC royalties during a country-by-country royalty term equal to a mid-teen percentage of annual net sales. The Company is required to pay KKC a double-digit percentage (less than 30%) of the payments that the Company receives from sublicensing of its rights under the KKC License Agreement, subject to certain exclusions. Avalo is responsible for the development and commercialization of AVTX-002 in all indications worldwide (other than the option in the KKC License Agreement that, upon exercise by KKC, allows KKC to develop, manufacture and commercialize AVTX-002 in Japan).

Market, Data, and Patent Exclusivity: Patents exclusively licensed from KKC may provide exclusivity in the United States through 2028 absent any extension, and additional patent applications filed by us covering certain methods of using AVTX-002, if issued and properly maintained, will provide additional exclusivity through 2043, absent any extension. Additionally, if we receive marketing approval, we expect to receive biologics data exclusivity in the United States, which would provide twelve years of data exclusivity in the United States from the date of licensing.

AVTX-007: ***Anti-IL-18 monoclonal antibody for treatment of Still's disease.***

Overview: AVTX-007 is a high affinity, fully human monoclonal antibody targeting the proinflammatory cytokine IL-18. We are developing AVTX-007 for the treatment of Still's Disease, including adult-onset Still's disease ("AOSD") and Systemic Juvenile Idiopathic Arthritis ("SJIA") (collectively, "Still's Disease").

About Still's disease: Still's disease is a rare inflammatory condition of unknown cause characterized by fever, sore throat, rash, and joint pain. AOSD refers to Still's disease in adult patients, while SJIA refers to Still's disease in pediatric patients. Elevated levels of IL-18 have been shown to be correlated with disease activity in patients with active Still's disease.

Competition: Nonsteroidal anti-inflammatory agents, corticosteroids and methotrexate may be used in the initial treatment of AOSD. Ilaris® (canakinumab) has been approved by the FDA for the treatment of active Still's disease, including AOSD and SJIA in patients aged 2 years and older in the United States. Additionally, Ilaris® and Kineret® (anakinra) have been approved by EMA for the treatment of Still's disease, including AOSD and SJIA in the European Union.

License: The Company has an exclusive global license to develop AVTX-007 from Medimmune Limited, a subsidiary of AstraZeneca plc ("AstraZeneca"). We paid an upfront license fee of $6 million in cash and equity. The Company is required to pay AstraZeneca up to an aggregate of $71.5 million based on the achievement of certain development and regulatory milestones. Upon commercialization, the Company is required to pay AstraZeneca sales-based milestone payments aggregating up to $90.0 million tied to the achievement of annual net sales targets. Additionally, the Company is also required to pay AstraZeneca royalties during a country-by-country royalty term equal to a tiered low double-digit percentage of annual net sales. Avalo is fully responsible for the development and commercialization of the program.

Market, Data, and Patent Exclusivity: Patents exclusively licensed from AstraZeneca may provide exclusivity in the United States through 2031, absent any extension, and additional patent applications filed by us covering certain methods of using AVTX-007, if issued and properly maintained, may provide additional exclusivity through 2042, absent any extension. AVTX-007 is eligible to receive orphan drug designation ("ODD") for the treatment of AOSD. Therefore, if we apply and are subsequently granted ODD in such an indication, following market approval, we may rely on a seven-year marketing exclusivity in the United States. Additionally, if we receive marketing approval, we expect to receive biologics data exclusivity in the United States, which may provide twelve years of data exclusivity in the United States from the date of licensing. AVTX-007 is also eligible to receive Orphan Designation ("OD") in the European Union. Therefore, if we apply and are subsequently granted OD in the European Union, we plan to rely on ten-year marketing exclusivity in the European Union.

AVTX-800 Programs: ***Monosaccharide therapies for treatment of select Congenital Disorders of Glycosylation.***

Overview: AVTX-801 and AVTX-803 are monosaccharide therapies with known therapeutic utility for the treatment of select congenital disorders of glycosylation ("CDGs"). Oral administration of AVTX-801 and AVTX-803 replenishes critical metabolic intermediates that are reduced or absent due to genetic mutations, overcoming single enzyme defects in respective CDGs to support glycoprotein synthesis, maintenance and function.

AVTX-801 is a D-galactose substrate replacement therapy for the treatment of phosphoglucomutase 1 ("PGM1") deficiency, also known as PGM1-CDG. AVTX-803 is a L-fucose substrate replacement therapy for the treatment of LADII, also known as SLC35C1-CDG.

About CDGs: CDGs are a group of rare, inherited, metabolic disorders caused by glycosylation defects that present as a broad range of clinical symptoms, depending on the mutation. Each mutation translates into a unique monosaccharide that is not able to be properly glycosylated onto proteins. This results in protein folding to be impaired and signs and symptoms can include significant pathology including coagulopathy, hepatopathy, myopathy, hypoglycemia, protein-losing enteropathy and reduced cell counts. CDG patients are born with a genetic defect that hinders their ability to utilize certain monosaccharides in the production of glycoproteins.

Designations of AVTX-800 Programs:

- ODD; the benefit of which, amongst other things, is a seven-year marketing exclusivity (upon approval) in the United States;
- Rare Pediatric Disease Designation ("RPDD"), which may qualify us to receive a priority review voucher ("PRV") upon FDA approval of each compound. If received, each PRV, which may be sold and transferred an unlimited amount of times, can be used to obtain priority review for a subsequent new drug application ("NDA") or biologics license application ("BLA"); and
- Fast Track Designation ("FTD"), which features actions to expedite the development of drugs that target serious or life-threatening conditions, including eligibility for expedited review and rolling review of each NDA by the FDA.

Competition: As of the date of this report, there are no FDA approved treatments for the treatment of CDGs (including PGM1-CDG, MPI-CDG or LADII), however dietary monosaccharide formulations have been shown to alleviate several of the clinical manifestations in CDG patients.

AVTX-801 and AVTX-803, are ultra-pure formulations of D-galactose and L-fucose, respectively. These formulations are naturally occurring substances contained in various foods, including dairy products and fruit. Additionally, D-galactose is also marketed by others as non-prescription dietary supplements.

Intellectual Property: The AVTX-800 programs were granted ODD by the FDA. As a result, at a minimum, following marketing approval, we plan to rely on seven-year marketing exclusivity in the United States.

Discovery Stage Assets

AVTX-008: In June 2021, the Company in-licensed a portfolio of issued patents and patent applications covering an immune checkpoint program (which we refer to as AVTX-008) from Sanford Burnham Prebys Medical Discovery Institute. The in-license further enhances the Company's development pipeline of novel biologics that address immunology and immuno-oncology targets.

Non-Core Pipeline Assets

AVTX-006: AVTX-006 is a dual mTORc1/c2 small molecule inhibitor for the treatment of complex lymphatic malformations. As a result of an ongoing portfolio prioritization review, we plan to pursue strategic alternatives for this program.

AVTX-802: AVTX-802 is a D-mannose substrate replacement therapy for the treatment of Mannose Phosphate Isomerase ("MPI") deficiency, also known as MPI-CDG. We are pausing current development of AVTX-802 due to an impasse related to FDA regulatory requirements of the trial design and feasibility based upon investigator feedback. We will re-evaluate development plans in the event of alignment with the FDA on the trial design.

AVTX-913: AVTX-913 is a protide nucleotide for the treatment of mitochondrial disorder. It is a preclinical asset and we may explore strategic alternatives.

Intellectual Property Overview

Our success depends in part on our ability to obtain and maintain proprietary protection for the technology and know-how upon which our products are based, to operate without infringing the proprietary rights of others and to prevent others from infringing our proprietary rights.

We hold ownership, trademark rights and/or exclusivity to develop and commercialize our products and product candidates covered by patents and patent applications. Our portfolio of patents includes patents or patent applications with claims directed to compositions of matter, including compounds, pharmaceutical formulations, methods of use, methods of manufacturing the compounds, or a combination of these claims. Depending upon the timing, duration and specifics of FDA approval of the use of a compound for a specific indication, some of our U.S. patents may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. Similar extensions to patent term may be available in other countries for particular patents in our portfolio.

We plan to augment our portfolio of compounds by focusing on the development (when possible) of new chemical entities ("NCEs") or biologics, which have not previously received FDA approval. Upon approval by the FDA, NCEs are entitled to market and data exclusivity in the United States with respect to generic drug competition for a period of five years from the date of FDA approval, even if the related patents have expired. Similarly, upon approval by the FDA, biologics are entitled to reference product exclusivity for a period of twelve years from the date of FDA approval, even if the related patents have expired.

Intellectual Property for specific pipeline assets, if applicable, are discussed above within the "Pipeline Assets" section.

Competition Overview

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies, both in the United States and abroad. We compete, or will compete, with existing and new products being developed by our competitors. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions that our research and development programs target. Some of these competitors also have greater resources and more experience than we do in regulatory development and marketing.

Competition for specific pipeline assets are discussed above within the "Pipeline Assets" section.

Manufacturing

We do not have any manufacturing facilities or personnel. We rely on contract manufacturing organizations to produce our drug candidates in accordance with applicable provisions of the FDA's current good manufacturing practices regulations ("cGMP") for use in our clinical studies. The manufacture of pharmaceuticals is subject to extensive good manufacturing practice ("GMP") regulations, which impose various procedural and documentation requirements and govern all areas of record keeping, production processes and controls, personnel and quality control.

Sales and Marketing

For our clinical stage pipeline assets, we may retain or partner in the United States with third parties on the commercialization rights and develop sales and marketing capabilities when needed. If we develop our own United States sales force we may complement it with co-promotion agreements with partners in and outside the United States. We may also seek to commercialize any of our approved products outside of the United States and may do so either through an expansion of our sales force or through collaboration with third parties.

Overall Competitive Climate and Risks

Other competitors may have a variety of drugs in development or may be awaiting FDA approval that could reach the market and become established before we have a product to sell. Our competitors may also develop alternative therapies that could limit the market for any drugs that we may develop. Many of our competitors are using technologies or methods different or similar to ours to identify and validate drug targets and to discover novel small compound drugs. Many of our competitors and their collaborators have significantly greater experience than we do in the following:

- identifying and validating targets;
- screening compounds against targets;
- preclinical and clinical trials of potential pharmaceutical products; and
- obtaining FDA and other regulatory clearances.

In addition, many of our competitors and their collaborators have substantially greater advantages in the following areas:

- capital resources;
- research and development resources;
- manufacturing capabilities; and
- sales and marketing.

Smaller companies might also prove to be significant competitors, particularly through proprietary research discoveries and collaborative arrangements with large pharmaceutical and established biotechnology companies. Many of our competitors have products that have been approved or are in advanced development. We face competition from other companies, academic institutions, governmental agencies and other public and private research organizations for collaborative arrangements with pharmaceutical and biotechnology companies, in recruiting and retaining highly qualified scientific and management personnel and for licenses to additional technologies. Our competitors, either alone or with their collaborators, may succeed in developing technologies or drugs that are more effective, safer, and more affordable or more easily administered than ours and may achieve patent protection or commercialize drugs sooner than us. Developments by others may render our product candidates or our technologies obsolete. Our failure to compete effectively could have a material adverse effect on our business.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export, pricing, and government contracting related to pharmaceutical products such as those we are developing.

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The process of obtaining marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, or other actions, such as the FDA's delay in review of or refusal to approve a pending NDA or BLA, withdrawal of an approval, imposition of a clinical hold or study termination, issuance of Warning Letters or Untitled Letters, mandated modifications to promotional materials or issuance of corrective information, requests for product recalls, consent decrees, corporate integrity agreements, deferred prosecution agreements, product seizures or detentions, refusal to allow product import or export, total or partial suspension of or restriction of or imposition of other requirements relating to production or distribution, injunctions, fines, debarment from government contracts and refusal of future orders under existing contracts, exclusion from participation in federal and state healthcare programs, FDA debarment, restitution, disgorgement or civil or criminal penalties, including fines and imprisonment.

FDA Marketing Approval

Obtaining FDA marketing approval for new products may take many years and require the expenditure of substantial financial resources. In order for the FDA to determine that a product is safe and effective for the proposed indication, the product must first undergo testing in animals (nonclinical studies). The data generated from nonclinical studies is used to support the filing of an Investigational New Drug Application (an "IND") under which human studies are conducted. Human testing is generally conducted under an IND in three phases following good clinical practice ("GCP") guidelines:

- Phase 1 studies evaluate the safety of the drug, generally in normal, healthy volunteers;
- Phase 2 studies evaluate safety and efficacy, as well as explore dosing ranges; these studies are typically conducted in patient volunteers who suffer from the particular disease condition that the drug is designed to treat; and
- Phase 3 studies evaluate safety and efficacy of the product at specific doses in one or more larger pivotal trials.

In addition to human testing, the manufacturing process of the potential product must be developed in accordance with GMP regulations. Prior to the approval of a new product, the FDA will inspect the facilities at which the proposed drug product is manufactured to ensure GMP compliance.

The cumulative safety and efficacy data generated from the clinical trials described above, chemistry, manufacturing and control ("CMC") information, nonclinical study data and proposed labeling are used as the basis to support approval of a marketing application (NDA or BLA) to the FDA. The preparation of an NDA or BLA requires the expenditure of substantial funds and the commitment of substantial resources. Additionally, in most cases, the submission of an NDA or BLA is subject to a substantial application user fee paid at the time of submission. The FDA conducts a preliminary administrative review upon receipt of the NDA or BLA submission. The FDA then either accepts the NDA or BLA for filing and commences its technical review or it refuses to accept the filing with the filer then having to address the deficiencies cited by the FDA and re-file the NDA or BLA again.

After evaluating the NDA or BLA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing, or other information, in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

The development and approval of new drugs requires substantial time, effort and financial resources. Data obtained from the development program are not always conclusive and may be susceptible to varying interpretations. These instances may delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us from marketing our products. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the product.

FDA Post-Approval Considerations

Drugs manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, manufacturing, periodic reporting, product sampling and distribution, advertising and promotion, and reporting of adverse experiences with the product and drug shortages. During the approval process, the FDA and the sponsor may agree that specific studies or clinical trials should be conducted as post-marketing commitments, but they are not required. The FDA may also impose post-marketing requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials and surveillance, to further assess and monitor the product's safety and effectiveness after commercialization. Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product becomes available in the market.

After approval, most changes to the approved product, such as manufacturing changes and adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are annual user fee requirements for any marketed products and new application fees for supplemental applications with clinical data. Additionally, the FDA strictly regulates the

labeling, advertising and promotion of products under an approved NDA or BLA. 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 marketed or promoted off-label uses may be subject to significant liability, including criminal and civil penalties under the FDCA and False Claims Act, exclusion from participation in federal healthcare programs, debarment from government contracts, refusal of future orders under existing contracts and mandatory compliance programs under corporate integrity agreements or deferred prosecution agreements.

Emergency Use Authorization

The FDA has the authority to grant an EUA to allow marketing and sale of unapproved medical products or unapproved uses of approved medical products in response to an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions, such as COVID-19, when there are no adequate, approved, and available alternatives. When issuing an EUA, the FDA imposes conditions of authorization, with which the company must comply. Such conditions include, but may not be limited to, compliance with labeling, distribution of materials designed to ensure proper use, reporting obligations, and restrictions on advertising and promotion. The EUA is only effective for the duration of the public health emergency, such as the ongoing COVID-19 pandemic. The FDA may revoke or terminate the EUA sooner if, for example, the company fails to comply with the conditions of authorization of the EUA or the drug is determined to be less effective or safe than it was initially believed to be.

Other Regulations of the Healthcare Industry

In addition to FDA regulations governing the marketing of pharmaceutical products, there are various other state and federal laws that may restrict business practices in the biopharmaceutical industry. These include the following:

- The federal Anti-Kickback laws and implementing regulations, which prohibit persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce either the referral of an individual, or furnishing or arranging for a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- Other Medicare laws, regulations, rules, manual provisions and policies that prescribe the requirements for coverage and payment for services performed by our customers, including the amount of such payment;
- The federal False Claims Act, which imposes civil and criminal liability on individuals and entities who submit, or cause to be submitted, false or fraudulent claims for payment to the government;
- The Foreign Corrupt Practices Act ("FCPA"), which prohibits certain payments made to foreign government officials;
- State and foreign law equivalents of the foregoing and state laws regarding pharmaceutical company marketing compliance, reporting and disclosure obligations;
- The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the "Affordable Care Act" or "ACA"), which among other things changes access to healthcare products and services; creates new fees for the pharmaceutical and medical device industries; changes rebates and prices for health care products and services; and requires additional reporting and *disclosure;*
- The Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and its implementing regulations (collectively, "HIPAA"), which creates federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program and which also imposes certain obligations on entities with respect to the privacy, security and transmission of individually identifiable health information; and
- The federal Physician Payment Sunshine Act, which requires certain pharmaceutical and biological manufacturers to engage in extensive tracking of payments or transfers of value to physicians and teaching hospitals and public reporting of the payment data.

If our operations are found to be in violation of any of these laws, regulations, rules or policies or any other law or governmental regulation, or if interpretations of the foregoing change, we may be subject to civil and criminal penalties, damages, fines, exclusion from the Medicare and Medicaid programs and the curtailment or restructuring of our operations.

To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals. This is currently not applicable as none of our products are currently sold in a foreign country.

Coverage and Reimbursement

The commercial success of our product candidates and our ability to commercialize any approved product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other third-party payers provide coverage for and establish adequate reimbursement levels for our therapeutic product candidates. In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payers are increasingly imposing additional requirements and restrictions on coverage, attempting to limit reimbursement levels or regulate the price of drugs and other medical products and services, particularly for new and innovative products and therapies, which often has resulted in average selling prices lower than they would otherwise be. For example, in the United States, federal and state governments reimburse covered prescription drugs at varying rates generally below average wholesale price. Federal programs also impose price controls through mandatory ceiling prices on purchases by federal agencies and federally funded hospitals and clinics and mandatory rebates on retail pharmacy prescriptions paid by Medicaid and Tricare. These restrictions and limitations influence the purchase of healthcare services and products. Legislative proposals to reform healthcare or reduce costs under government programs may result in lower reimbursement for our product candidates or exclusion of our product candidates from coverage. Moreover, the Medicare and Medicaid programs increasingly are used as models for how private payers and other governmental payers develop their coverage and reimbursement policies.

In addition, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and utilization, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, competition within therapeutic classes, availability of generic equivalents, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, coverage and reimbursement policies and pricing in general. The cost containment measures that healthcare payers and providers are instituting and any healthcare reform implemented in the future could significantly reduce our revenues from the sale of any approved product candidates. We cannot provide any assurances that we will be able to obtain and maintain third-party coverage or adequate reimbursement for our product candidates in whole or in part.

Healthcare Reform

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system. The United States government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

In recent years, Congress has considered reductions in Medicare reimbursement levels for drugs administered by physicians. CMS, the agency that administers the Medicare and Medicaid programs, also has authority to revise reimbursement rates and to implement coverage restrictions for some drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payers.

The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. The Affordable Care Act was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers, and impose additional health policy reforms. Since its passage, there have been significant ongoing efforts to modify or eliminate the Affordable Care Act.

On January 20, 2017, President Trump signed an executive order directing federal agencies to exercise existing authorities to reduce burdens associated with the Affordable Care Act pending further action by Congress. In October 2017, he signed an Executive Order which directed federal agencies to modify how the Affordable Care Act is implemented. The Tax Cuts and Jobs Act (the "TCJA"), enacted on December 22, 2017, repealed the shared responsibility payment for individuals who fail to maintain minimum essential coverage under section 5000A of the Internal Revenue Code of 1986, as amended (the "IRC"), as amended, commonly referred to as the individual mandate. While the Biden administration has rolled back many of the executive orders issued by former President Trump and has stated that it intends to build on the ACA and to expand coverage thereunder, ongoing repeal and reform efforts impacting the ACA and the healthcare sector more broadly are likely.

Other legislative changes have been proposed and adopted since passage of the Affordable Care Act. The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than $1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year, which went into effect in April 2013. Subsequent litigation extended the 2% reduction, on average, to 2030 unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act"), the 2% Medicare sequester reductions were suspended from May 1, 2020 through March 31, 2021 due to the COVID-19 pandemic. On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further legislative and regulatory changes under the Affordable Care Act remain possible, although the new Administration under President Biden has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for subsidies under it. It is unknown what form any such changes or any law would take, and how or whether it may affect our business in the future. We expect that changes or additions to the Affordable Care Act, the Medicare and Medicaid programs, changes allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

The Affordable Care Act has also been subject to challenges in the courts, which remain ongoing.

The Affordable Care Act requires pharmaceutical manufacturers of branded prescription drugs to pay a branded prescription drug fee to the federal government. Each individual pharmaceutical manufacturer pays a prorated share of the branded prescription drug fee, based on the dollar value of its branded prescription drug sales to certain federal programs identified in the law. Furthermore, the law requires manufacturers to provide a 50% discount off the negotiated price of prescriptions filled by beneficiaries in the Medicare Part D coverage gap, referred to as the "donut hole." The Bipartisan Budget Act of 2018 (the "BBA"), among other things, amended the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole," by increasing from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D.

Payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives as well. For example, CMS may develop new payment and delivery models, such as bundled payment models. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for pharmaceutical products.

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

We expect that additional federal, state and foreign healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, once approved, or additional pricing pressures.

The Foreign Corrupt Practices Act

The FCPA prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

Exclusivity and Approval of Competing Products

Hatch-Waxman Patent Exclusivity

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a NDA, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application ("ANDA") or 505(b)(2) NDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the listed drug and has been shown to be bioequivalent through *in vitro* or *in vivo* testing or otherwise to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

The ANDA or 505(b)(2) NDA applicant is required to provide a certification to the FDA in the product application concerning any patents listed for the approved product in the FDA's Orange Book, except for patents covering methods of use for which the applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

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

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except when the ANDA or 505(b)(2) NDA applicant challenges a listed patent or if the listed patent is a patented method of use for which approval is not being sought. A certification that the proposed product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or does not indicate that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA or 505(b)(2) NDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of notice of the Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) NDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, a decision in the infringement case that is favorable to the ANDA applicant or other period determined by a court.

Hatch-Waxman Non-Patent Exclusivity

Market and data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications for competing products. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. However, an ANDA or 505(b)(2) NDA may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA or 505(b)(2) NDA, if new clinical investigations other than bioavailability studies that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application or supplement. Three-year exclusivity may be awarded for changes to a previously approved drug product, such as new indications, dosages, strengths or dosage forms of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and, as a general matter, does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full

NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Approval of Biosimilars and Biologic Exclusivity

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which was enacted as part of the Affordable Care Act, created an abbreviated approval pathway for biological products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-licensed reference biological product via an approved BLA. Biosimilarity to an approved reference product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity is demonstrated in steps beginning with rigorous analytical studies or "fingerprinting", in vitro studies, in vivo animal studies, and generally at least one clinical study, absent a waiver from the Secretary of Health and Human Services. The biosimilarity exercise tests the hypothesis that the investigational product and the reference product are the same. If at any point in the stepwise biosimilarity process a significant difference is observed, then the products are not biosimilar, and the product will have to developed and approved using a traditional NDA or BLA. In order to meet the higher hurdle of interchangeability, a sponsor must demonstrate that the biosimilar product can be expected to produce the same clinical result as the reference product, and for a product that is administered more than once, that the risk of switching between the reference product and biosimilar product is not greater than the risk of maintaining the patient on the reference product. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being evaluated by the FDA.

Upon approval of a BLA, the biologic is listed in the Purple Book along with the date it was licensed; whether the biological product licensed has been determined by the FDA to be biosimilar to or interchangeable with a reference biological product (an already-licensed FDA biological product) and the date of expiration of applicable exclusivity. Under the BPCIA, a reference biologic is granted 12 years of exclusivity from the time of first licensure of the reference product. This 12-year period includes 4 years before the FDA may accept for filing an application for a biologic that references a branded (reference) product.

Pediatric Exclusivity.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent exclusivity period described above. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve an ANDA or 505(b)(2) application owing to regulatory exclusivity or listed patents.

Orphan Drug Designation and Exclusivity.

The Orphan Drug Act provides incentives for the development of drugs intended to treat rare diseases or conditions, which generally are diseases or conditions affecting less than 200,000 individuals annually in the United States, or affecting more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making the drug available in the United States will be recovered from United States sales. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain orphan designation if there is a drug already approved by the FDA that is intended for the same indication and that is considered by the FDA to be the same drug as the already approved drug. Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical study costs, tax advantages, and user-fee waivers. In addition, if a product receives FDA approval for the indication for which it has orphan designation, the product is generally entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

Rare Pediatric Disease Designation

Under Section 529 to the FDCA, the FDA will award PRVs to sponsors of rare pediatric disease product applications that meet certain criteria. Under this program, a sponsor who receives an approval for a drug or biologic for a rare pediatric disease may qualify for a PRV that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The PRV may be sold or transferred an unlimited number of times. Under the PRV program, any drug that is granted RPDD by September 30, 2024 and receives approval by September 20, 2026 may qualify for a PRV.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding drug development and commercialization. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. The processes for obtaining marketing approvals in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

European Union Drug Approval Process

To obtain a marketing authorization of a drug in the European Union, we may submit marketing authorization applications ("MAAs") either under the so-called centralized or national authorization procedures.

Centralized procedure

The centralized procedure provides for the grant of a single marketing authorization following a favorable opinion by the EMA that is valid in all European Union member states, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of specified diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions. The centralized procedure is optional for products that represent a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health. Under the centralized procedure the maximum timeframe for the evaluation of an MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee of Medicinal Products for Human Use ("CHMP"). Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is of 150 days, excluding stop-clocks.

National authorization procedures

There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:

- **Decentralized procedure.** Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.

- **Mutual recognition procedure.** In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In the European Union, new products authorized for marketing (i.e., reference products) qualify for eight years of data exclusivity and an additional two years of market exclusivity upon marketing authorization. The data exclusivity period prevents generic applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic marketing authorization in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic applicant from commercializing its product in the EU until ten years have elapsed from the initial authorization of the reference product in the EU. The ten-year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Commercially Marketed Product

The Company currently has one marketed product, Millipred®, an oral prednisolone indicated across a wide variety of inflammatory conditions and indications. Prednisolone is a man-made form of a natural substance (corticosteroid hormone) made by the adrenal gland. It is used to treat conditions such as arthritis, blood disorders, immune system disorders, skin and eye conditions, respiratory disorders, cancer, and severe allergies. Prednisolone decreases an individual's immune response to various diseases to reduce symptoms such as pain, swelling and allergic-type reactions. Millipred® is supplied in 5mg tablets.

Millipred® tablets primarily compete in the generic prednisolone market. We believe our primary point of differentiation is that we offer the lowest strength prednisolone in the marketplace allowing healthcare professionals greater flexibility when dosing a glucocorticoid steroid across a variety of pediatric and adult indications. Additionally, Millipred® utilizes the proprietary double taste-masking technology to provide a pleasant grape taste with no bitterness, which makes the product easier to administer to children.

Aytu BioScience, Inc. ("Aytu"), to which the Company sold its rights, title and interests in assets relating to certain commercialized products in 2019, managed Millipred® commercial operations through August 31, 2021 pursuant to transition service agreements. In the third quarter of 2021, the Company finalized its own trade and distribution channel to allow it to control third party distribution for Millipred® and began managing Millipred® commercial operations at that time.

Employees and Human Capital Management

As of December 31, 2021, we had forty-four employees, forty-two of whom are full-time and two of whom are part-time. Twenty-eight of our employees were primarily engaged in research and development activities. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

We believe that our future success largely depends upon our continued ability to attract and retain highly skilled and qualified personnel. We believe that we provide our employees with competitive salaries and bonuses, opportunities for equity ownership, and an employment package that promotes well-being across all aspects of their lives, including health care, retirement planning and paid time off. We value diversity and inclusiveness at all levels.

Corporate Information

We were incorporated in Delaware in 2011 and commenced operations in the second quarter of 2011. Our principal executive offices are located at 540 Gaither Road, Suite 400, Rockville, Maryland 20850, and our phone number is (410) 522-8707. Our website address is www.avalotx.com. The information on, or that can be accessed through, our website is not part of this report.

Available Information

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (the "Exchange Act"), are available free of charge on our website at www.avalotx.com as soon as reasonably practicable after electronically filing or furnishing such material to the Securities and Exchange Commission. The Securities and Exchange Commission maintains a website (www.sec.gov) that includes our reports, proxy statements and other information.

Item 1A. Risk Factors.

You should consider carefully the following information about the risks described below, together with the other information contained in this Annual Report on Form 10-K and in our other public filings, in evaluating our business. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our warrants and common stock would likely decline.

Risks Related to Our Financial Position and Capital Needs

We will need substantial additional capital for the continued development of our product candidates and for our long-term operations.

We will need to raise capital to continue product development. Our capital requirements depend on many factors, including:

- the rate and level of patient recruitment into clinical trials, particularly those in Phase 2 and Phase 3 stages of development;
- the level of research and development investment required to develop product candidates;
- changes in product development plans needed to address any difficulties that may arise in manufacturing, preclinical activities, clinical trials or commercialization;
- revenue from sales of Millipred;
- the ability and willingness to enter into new agreements with strategic partners, and the terms of these agreements;
- the success rate in pre-clinical and clinical efforts;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution;
- proceeds, if any, from sales of any PRV received;
- revenue, if any, received from commercial sales of product candidates, should any of our product candidates receive marketing approval;
- the effect of competing product and market developments;
- the timing and amount of milestone payments we are required to make under license agreements;
- in-licensing and/or acquisition or other transaction costs (if any) for potential product development candidates;
- time and costs involved in obtaining regulatory approvals; and
- costs of filing, prosecuting, defending, and enforcing patent claims and other intellectual property rights.

We will likely require significant amounts of additional capital in the future, and such capital might not be available on favorable terms when needed, if at all. Furthermore, our ability to raise capital on a timely basis through the issuance and sale of equity securities might be limited by Nasdaq's listing rules on transactions that do not qualify as "public offerings" (as defined in Nasdaq listing rules), which might require us to obtain stockholder approval prior to the issuance of common stock (or securities convertible into or exercisable for common stock) at a price per share that is less than the "Minimum Price" if the issuance would equal 20% or more of our common stock outstanding before the issuance.

We might never progress to the point where we have commercially successful product sales or other revenue sufficient to sustain operations. Accordingly, we may seek to raise these funds through public or private equity offerings, debt financings, credit facilities, partnering or other corporate collaborations and licensing arrangements. If adequate funds are not available or are not available on acceptable terms, our ability to fund our operations, take advantage of opportunities, develop products and technologies, and otherwise respond to competitive pressures could be significantly delayed or limited, and we might need to downsize or halt our operations.

Our current revenue depends on one product, which is not sufficient to provide adequate capital for the continued development of our product candidates and therefore could require us to raise additional financing.

Following the sale of our pediatric portfolio, namely the rights to Aciphex® Sprinkle™, Cefaclor for Oral Suspension, Karbinal™ ER, Flexichamber™, Poly-Vi-Flor® and Tri-Vi-Flor™ to Aytu in 2019, we currently have rights to only one commercial pharmaceutical product, Millipred. We do not expect Millipred, which we consider a non-core asset, to generate significant revenue and profits, but we currently rely on it for all our commercial revenue. We entered into an amendment related to the underlying Millipred license and supply agreement in the fourth quarter of 2020, which extends the original agreement for a period of thirty months (from April 1, 2021 through September 30, 2023). Beginning July 1, 2021, Avalo is required to pay fifty percent of the net profit of the Millipred product following each calendar quarter, subject to a $0.5 million quarterly minimum payment.

Aytu managed Millipred® commercial operations until August 31, 2021 pursuant to transition service agreements, which included managing the third-party logistics provider and providing accounting reporting services. Aytu collected cash on behalf of Avalo for revenue generated by sales of Millipred from the second quarter of 2020 through the third quarter of 2021 and is obligated to transfer the cash generated by such sales. In the third quarter of 2021, Avalo finalized its trade and distribution channel to allow it to control third party distribution and began managing commercial operations at that time.

The current transition service agreement allows Aytu to withhold cash of $2,000,00 until September 30, 2022 and $1,000,000 until December 1, 2024. The full amount is due to Avalo on December 1, 2024. Adverse economic conditions or financial difficulties of Aytu could impair its ability to remit such payments or could cause Aytu to delay such payments. If Aytu were unable to meet its obligations, it could consider restructuring under the bankruptcy laws, which might make it difficult for us to collect all or a significant portion of the cash owed to us by Aytu. Our inability to collect the accounts receivable to our revenues generated by Millipred® from Aytu could adversely affect our cash flows, financial condition, and results of operations. Furthermore, the transition of control of the commercial operation of Millipred that occurred in the third quarter of 2021 could cause disruptions in Millipred sales or other negative operational issues.

Our operations might not produce significant revenues in the near term, or at all, which might harm our ability to obtain additional financing and might require us to reduce or discontinue our operations. You must consider our business and prospects in light of the risks and difficulties we will encounter as a company operating in a rapidly evolving industry. We might not be able to successfully address these risks and difficulties, which could significantly harm our business, operating results, and financial condition.

Our ability to increase revenue in the future will depend on developing and commercializing our current clinical pipeline of product candidates. Identifying, developing, obtaining regulatory approval and commercializing product candidates is prone to the risks of failure inherent in clinical development. Developing product candidates is expensive, and we expect to spend substantial amounts as we fund our product development. We cannot provide any assurance that we will be able to successfully advance any product candidates through the development process or successfully commercialize any product candidates, or that any such product candidate will be widely accepted in the marketplace or be more effective than other commercially available alternatives. Any failure to develop or commercialize a product candidate in our current clinical pipeline could require us to raise additional financing.

The ongoing COVID-19 pandemic has had an impact on our business operations and clinical trials and could continue, directly or indirectly, to adversely affect our business, results of operations and financial condition and our stock price.

The COVID-19 pandemic has had an impact on our business operations and we continue to monitor applicable government recommendations. We have made modifications to our normal operations because of the COVID-19 pandemic, including allowing our employees to work remotely. Notwithstanding these measures, the COVID-19 pandemic could affect the health and availability of our workforce as well as those of the third parties whom we are relying on to take similar measures. For example, we have seen the interruption of, or delays in receiving, supplies of our research and clinical trial materials due to among other things, staffing shortages, production slowdowns or stoppages, or shortages in raw materials because of ongoing efforts to address the COVID-19 pandemic. The extent and severity of the future impact on our business and clinical trials will be determined largely by the extent of disruptions in the supply chains for our research and clinical trial materials, such as committed manufacturing slots being reallocated to other customers of our contract manufacturers pursuant to government orders under the Defense Production Act, and by delays in the conduct and recruitment of current and future clinical trials. These impacts of COVID-19 could affect our other ongoing clinical trials and delay their timelines.

The continued spread of COVID-19 globally could adversely impact our clinical trial operations in the United States and in Europe, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. In addition, if the FDA elects to delay face-to-face meetings for an extended period of time, we may have to delay the initiation of any additional clinical trials for which we require additional approval from the FDA, or, if we are seeking to commercialize our product candidates, such delay could force us to delay commercialization. Any decision by the FDA to delay meeting with us in light of COVID-19 could have a material adverse effect on our scheduled clinical trials or on our efforts to obtain commercialization approval, which could increase our operating expenses and have a material adverse effect on our financial results.

Moreover, COVID-19 may also affect employees of third-party contract research organizations located in affected geographies that we rely upon to carry out such enrollments and trials. Any negative impact COVID-19 has to patient enrollment or treatment could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

Although it is not possible at this time to estimate the entirety of the impact that the COVID-19 pandemic will have on our business, operations and employees, our contract manufacturers, our clinical research contractors, and our collaborators in clinical research, any continued spread of COVID-19, measures taken by governments, actions taken to protect employees from this disease, and the broad impact of the pandemic on all business activities and financial markets, may materially and adversely affect our business, results of operations and financial condition and our stock price.

We might require additional capital to continue to fund our operations and to finance the further advancement of our product candidates, which might not be available to us on acceptable terms, or at all. Failure to obtain any necessary capital will force us to delay, limit or terminate our product development efforts or cease our operations.

At December 31, 2021, we had $54.6 million in cash and cash equivalents and $19.9 million in current liabilities. Accordingly, we might not currently have sufficient funds to finance our continuing operations beyond the short term or to further advance any of our product candidates.

As a research and development company, our operations have consumed substantial amounts of cash since inception. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance our product candidates into clinical trials or obtain and advance additional product candidates. Circumstances may cause us to consume capital more rapidly than we currently anticipate. We may need to raise additional funds or otherwise obtain funding through collaborations if we choose to initiate additional clinical trials for product candidates.

Additional fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we do not raise additional capital when required or on acceptable terms, we may need to:

- significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates or cease operations altogether;
- seek strategic alliances for research and development programs at an earlier stage than we would otherwise desire or on terms less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize itself.

Our future funding requirements, both short and long term, will depend on many factors, including:

- the initiation, progress, timing, costs and results of preclinical and clinical studies for our product candidates and future product candidates we may develop;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more studies than we currently expect to perform;
- the cost to establish, maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- the effect of competing technological and market developments;
- market acceptance of any approved product candidates;
- the costs of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost and timing of selecting, auditing and potentially validating a manufacturing site for commercial-scale manufacturing; and
- the cost of developing our sales, marketing and distribution capabilities to accommodate any of our product candidates for which we receive marketing approval and that we determine to commercialize ourselves or in collaboration with our partners.

Under our Loan Agreement, our Lenders have broad discretion as to what qualifies as a Material Adverse Change that could cause the loan amounts due to be accelerated, thus exposing us to illiquidity. The limitations under our Loan Agreement may also restrict our operations or produce other adverse results.

Our current loan agreement (the "Loan Agreement") with Horizon Technology Finance Corporation and Powerscourt Investments XXV, LP (collectively, the "Lenders"), which we entered into in June 2021, contains a variety of affirmative and negative covenants, including required financial reporting, limitations on certain dispositions of assets, limitations on the incurrence of additional debt and other requirements. The Loan Agreement also gives the Lenders the right to declare an event of default and accelerate the loan amounts due under the Loan Agreement if there has been a material adverse change in the business, including a change which results in a material impairment in our prospect of repayment of any portion of the loan amounts or the value or priority of the Lenders' security interest in the collateral. To secure our performance of our obligations under this Loan Agreement, we granted a security interest in substantially all of our assets, other than certain intellectual property assets, to the Lenders. Our failure to comply with the

covenants in the Loan Agreement, the occurrence of an adverse change as described above or the occurrence of certain other specified events could result in an event of default that, if not cured or waived, could result in the acceleration of all or a substantial portion of our debt, potential foreclosure on our assets and other adverse results. Additionally, we are bound by certain negative covenants setting forth actions that are not permitted to be taken during the term of the Loan Agreement without consent of the Lenders, including, without limitation, incurring certain additional indebtedness, making certain asset dispositions, entering into certain mergers, acquisitions or other business combination transactions or incurring any non-permitted lien or other encumbrance on our assets. The foregoing prohibitions and constraints on our operations could result in our inability to: (i) acquire promising intellectual property or other assets on desired timelines or terms; (ii) reduce costs by disposing of assets or business segments no longer deemed advantageous to retain; (iii) stimulate further corporate growth or development through the assumption of additional debt; or (iv) enter into other arrangements that necessitate the imposition of a lien on corporate assets. We cannot assure you that our business will be able to generate sufficient cash flow or that future borrowings or other financings will be available to us in an amount sufficient to enable us to pay the principal, premium, if any, and interest on our existing or future indebtedness.

Servicing our debt requires a significant amount of cash, and we might not have or be able to obtain sufficient cash to pay our substantial debt.

As of December 31, 2021, we had $36.1 million aggregate principal outstanding under our Loan Agreement. Our ability to make scheduled payments on our indebtedness depends on our future performance, which is subject to many factors beyond our control. If we are unable to service our debt, we may be required to adopt one or more alternatives, such as selling assets, restructuring debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. In addition, our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time. We might not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default and acceleration of our debt obligations.

Our role as a guarantor of Certain Obligations assigned to Aytu exposes us to risk of loss or illiquidity.

In connection with the Aytu Divestiture, as defined in the Notes to our Consolidated Financial Statements, Aytu assumed our financial obligations to Deerfield CSF, LLC ("Deerfield"), which includes the remaining contingent consideration related to future royalties on the divested products. Aytu publicly reported that it had entered into a Waiver, Release, and Consent in June 2021, pursuant to which it paid a portion of the contingent consideration early and agreed to pay the remaining fixed obligations of $3 million in six equal quarterly payments of $0.5 million commencing September 1, 2021 (the "Deerfield Obligation"). The Deerfield Obligation could be accelerated upon default or a breach of covenants.

We also assigned payment obligations ("TRIS Obligations") to Aytu under a supply and distribution agreement (the "Karbinal Agreement") with TRIS Pharma Inc ("TRIS"), which includes a per-unit royalty make whole payment for each unit sold under an annual minimum sales commitment through 2025. The total future make-whole payments to be made by Aytu are unknown as the amount owed to TRIS is dependent on the number of units sold.

As a part of these assignments, we also became a guarantor to the Deerfield Obligation and TRIS Obligations. If Aytu defaults under the terms of the agreement with Deerfield or TRIS, we could be liable as a guarantor for unpaid amounts of the Deerfield Obligation and the TRIS Obligation. Any amount we would be required to pay under the remaining Deerfield Obligation and the TRIS Obligation would limit the amount of cash available for development of our clinical pipeline and may expose us to significant losses, which would materially and adversely affect our results of operations.

We have incurred significant net losses in most periods since our inception and we expect to continue to incur net losses in the future.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate an adequate effect or acceptable safety profile, gain marketing approval and become commercially viable. Historically, we financed our operations primarily through public and private equity offerings. We incurred a net loss of $84.4 million for the year ended December 31, 2021. As of December 31, 2021, we had an accumulated deficit of $262.2 million. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development program and from general and administrative costs associated with our operations.

We expect to continue to incur losses in the future and we might never achieve profitability on an annual basis. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. Our future profitability will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

We have a significant amount of gross net operating losses ("NOLs") for federal and state purposes. The NOLs accumulated through the end of 2017 will begin to expire in 2031. Unused NOLs for the current tax year and prior tax years will carry forward to offset future taxable income, if any, until such unused losses expire. Unused NOLs generated after December 31, 2017, will not expire and may be carried forward indefinitely but will be only deductible to the extent of 80% of current year taxable income in any given year. In addition, both the deductibility of current and future unused NOL carryovers may be subject to limitation under Sections 382 and 383 of the IRC. Sections 382 and 383 of the IRC subject the future utilization of NOLs and certain other tax attributes, such as research and experimental tax credits, to an annual limitation in the event of certain ownership changes. In general, an "ownership change" is defined as a greater than 50% change (by value) in equity ownership over a three-year period).

Our operating results fluctuate from quarter to quarter and year-to-year, making future operating results difficult to predict.

Our quarterly and annual operating results historically have fluctuated and are likely to continue to fluctuate depending on several factors, many of which are beyond our control. Accordingly, our quarterly and annual results are difficult to predict prior to the end of the quarter or year, and we may be unable to confirm or adjust expectations with respect to our operating results for a particular period until that period has closed. In the event we provide cash projections or other guidance, any failure to meet such targets or failure to meet the expectations of analysts could adversely impact the market price of our securities. Therefore, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to the Discovery and Development of Our Product Candidates

Our product candidates that we intend to commercialize are in early stages of development. If we do not successfully complete preclinical testing and clinical development of our product candidates or experience significant delays in doing so, our business may be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification and preclinical and clinical development of product candidates. Our ability to increase product revenues will depend on our ability to advance our clinical product candidates towards approval and our preclinical product candidates into clinical development. The outcome of preclinical studies and earlier clinical trials might not predict the success of future clinical trials. Preclinical data and clinical trial data may be susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and early clinical trials have nonetheless failed in later clinical development. Our inability to successfully complete development of our product candidates could result in additional costs to us relating to product development and obtaining marketing approval and impair our ability to generate product revenues and commercialization and sales milestone payments and royalties on product sales.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining required approvals from regulatory authorities for the sale of future product candidates, we alone, or with a partner, must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive and difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials might not predict the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to lack of efficacy or unacceptable safety profiles, notwithstanding promising results in earlier trials. Our product candidates will require additional clinical and preclinical development, management of clinical, preclinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply on our own or from a third party, expansion of our commercial organization, and substantial investment and significant marketing efforts before we generate any revenues from sales of any of those product candidates approved for marketing. We do not know whether the clinical trials we or our partners may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market any of our product candidates in any particular jurisdiction or jurisdictions. If later stage clinical trials do not produce favorable results, our ability to achieve regulatory approval for any of our product candidates would be adversely impacted.

If we experience delays in clinical testing, we will be delayed in obtaining regulatory approvals and commercializing our product candidates, our costs may increase and our business may be harmed.

We do not know whether any clinical trials will begin as planned, whether the design will be revised prior to or during conduct of the study, completed on schedule or conducted at all. Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may harm our business, results of operations and prospects.

Events which may result in a delay or unsuccessful completion of clinical development include:

- delays in reaching an agreement with or failure in obtaining authorization from the FDA, other regulatory authorities or institutional review boards ("IRBs") to commence or amend a clinical trial;
- delays in reaching agreements with the FDA regarding requisite trial design or endpoints sufficient to establish a clinically meaningful benefit of our product candidates given there might not be well-established development paths and outcomes;
- inability to agree with the FDA on operationally viable endpoints or trial design;
- imposition of a clinical hold or trial termination following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities, or due to concerns about trial design, or a decision by the FDA, other regulatory authorities, IRBs or the company, or recommendation by a data safety monitoring board, to place the trial on hold or otherwise suspend or terminate clinical trials at any time for safety issues or for any other reason;
- delays in reaching agreement on acceptable terms with prospective contract research organizations ("CROs") and clinical trial sites;

- deviations from the trial protocol by clinical trial sites and investigators, or failing to conduct the trial in accordance with regulatory requirements;
- failure of our third parties, such as CROs, to satisfy their contractual duties or meet expected deadlines;
- failure to enter into agreements with third parties to obtain the results of clinical trials;
- delays in the importation and manufacture of clinical supply;
- delays in the testing, validation and delivery of the clinical supply of the product candidates to the clinical sites;
- for clinical trials in selected subject populations, delays in identification and auditing of central or other laboratories and the transfer and validation of assays or tests to be used to identify selected subjects;
- delays due to the world-wide shortage of animal testing subjects, including monkeys;
- delays in recruiting suitable subjects to participate in a trial;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- delays caused by subjects dropping out of a trial due to side effects or disease progression;
- delays in adding new investigators and clinical trial sites;
- delays resulting from the ongoing COVID-19 pandemic;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials; or
- changes in government regulations or administrative actions or lack of adequate funding to continue the clinical trials.

Any inability by us or our partners to timely complete clinical development could result in additional costs to us relating to product development and obtaining marketing approval and impair our ability to generate product revenues and commercialization and sales milestone payments and royalties on product sales.

If we are unable to enroll appropriate subjects in clinical trials or retain patients in the clinical trials we perform, we will be unable to complete these trials on a timely basis or at all.

Identifying and qualifying subjects to participate in clinical trials of our product candidates, and retaining the subjects once qualified, is critical to our success. The timing of our clinical trials depends on the speed at which we can recruit appropriate subjects to participate in testing our product candidates as well as completion of required follow-up periods. If subjects are unwilling to participate in our trials, the timeline for recruiting subjects, conducting trials and obtaining marketing approval of potential products may be delayed.

Difficulty or delays in patient recruitment into our trials could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether. Many factors affect subject enrollment, including:

- the size and nature of the subject population;
- the number and location of clinical sites we enroll;
- the proximity of subjects to clinical sites;
- perceived risks and benefits of the product candidate under trial;
- competition with other companies for clinical sites or subjects;
- competing clinical trials;
- the eligibility and exclusion criteria for the trial;
- the design of the clinical trial;
- effectiveness of publicity for the clinical trials;
- inability to obtain and maintain subject consents;
- ability to monitor subjects adequately during and after the administration of the product candidate and the ability of subjects to comply with the clinical trial requirements;
- risk that enrolled subjects will drop out or be withdrawn before completion; and
- clinicians' and subjects' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance. If we are unable to enroll sufficient subjects in our clinical trials, if enrollment is slower than we anticipate, or if our clinical trials require more subjects than we anticipate, our clinical trials may be delayed or might not be completed. If we experience delays in our clinical trials, the commercial prospects of our product candidates will be harmed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and

generate revenues. In addition, many of the factors that could cause a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our lead product candidates or our other product candidates.

Furthermore, because several of our programs are focused on the treatment of patients with rare genetic diseases, our ability to enroll eligible patients in these trials may be limited or slower than we anticipate in light of the small patient populations involved and the specific age range required for treatment eligibility in some indications. In addition, our potential competitors, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions, may seek to develop competing therapies, which would further limit the small patient pool available for our studies.

Completion of orphan clinical trials may take considerably more time than other trials, sometimes years, depending on factors such as type, complexity, novelty and intended use of a product candidate. As a result of the uncertainties described above, there can be no assurance that we will meet timelines that we establish for any of our rare clinical trials.

We may fail to successfully identify, in-license, acquire, develop or commercialize potential product candidates.

The success of our business depends in part upon our ability to identify and validate new therapeutic targets and identify, develop and commercialize therapeutics, which we may develop ourselves, in-license or acquire from others. Research programs designed to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research efforts may initially show promise in identifying potential therapeutic targets or candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- Our methodology, including our screening technology, might not successfully identify medically relevant potential product candidates;
- Our competitors may develop alternatives that render our product candidates obsolete;
- We may encounter product manufacturing difficulties that limit yield or produce undesirable characteristics that increase the cost of goods, cause delays or make the product candidates unmarketable;
- Our product candidates may cause adverse effects in subjects, even after successful initial toxicology studies, which may make the product candidates unmarketable;
- Our product candidates might not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- Our product candidates might not demonstrate a meaningful benefit to subjects;
- Our potential collaboration partners may change their development profiles or plans for potential product candidates or abandon a therapeutic area or the development of a partnered product; and
- Our reliance on third party clinical trials may cause us to be denied access to clinical results that may be significant to further clinical development.

Additionally, we may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful. 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, operating results and prospects and could potentially cause us to cease operations.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their marketing approval, limit the commercial profile of an approved label, or result in significant negative consequences following any marketing approval.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to issue a clinical hold and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or other comparable foreign regulatory authority. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics.

Should our clinical studies of our product candidates reveal undesirable side effects, we could suspend or terminate our trials or the FDA or comparable foreign regulatory authorities as well as IRBs could order us to suspend or cease clinical trials. The FDA or comparable regulatory authorities could also deny approval of our product candidates for any or all targeted indications or only for a limited indication or patient population or could require label warnings, contraindications or precautions, including black box warnings, post-market studies, testing and surveillance programs or other conditions including distribution restrictions or other risk management mechanisms under a costly risk evaluation and mitigation strategy ("REMS"). Drug-related side effects could affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Additionally, if one or more of our product candidates receives marketing approval, and we or others (regulatory agencies, consumers, etc.) later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- We may suspend marketing of, or withdraw or recall, such product;
- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label or other label modifications;
- the FDA or other regulatory bodies may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;
- the FDA or comparable foreign regulatory authorities may require the establishment or modification of a REMS or other restrictions on marketing and distribution, or a comparable foreign regulatory authority may require the establishment or modification of a similar strategy that may, for instance, require us to issue a medication guide outlining the risks of such side effects for distribution to patients or restrict distribution of our products and impose burdensome implementation requirements on us;
- regulatory authorities may require that we conduct post-marketing studies; and
- We could be sued and held liable for harm caused to subjects or patients.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate or otherwise materially harm the commercial prospects for the product candidate, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

Changes in product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates are developed through preclinical studies to late-stage clinical trials towards regulatory approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, FDA or comparable foreign regulatory authorities notification or approval.

Similarly, changes in the location of manufacturing or addition of manufacturing facilities may increase our costs and require additional studies and FDA approval. This may require us to ensure that the new facility meets all applicable regulatory requirements, is adequately validated and qualified, and to conduct additional studies of product candidates manufactured at the new location. Any of the above could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay regulatory approval of our product candidates and jeopardize our ability to commence product sales and generate revenue.

Biologic products are highly complex and expensive, and if the third-party manufacturers we contract with are unable to provide quality and timely offerings to our clinical trial sites, our clinical trials might be delayed.

The process of manufacturing biologics and their components is complex, expensive, highly-regulated and subject to multiple risks.

Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. Furthermore, the development of biologic products involves a lengthy and expensive process with an uncertain outcome, which might require us to incur additional unforeseen costs to complete our clinical trials.

Although we are working with third parties to develop reproducible and commercially viable manufacturing processes for our product candidates, doing so is a difficult and uncertain task, and there are risks associated with scaling to the level required for advanced clinical trials or commercialization, including, among others, cost overruns, potential problems with process scale-out, process reproducibility, stability issues, lot consistency, and timely availability of reagents or raw materials.

We may make changes as we continue to evolve the manufacturing processes for our product candidates for advanced clinical trials and commercialization, and we cannot be sure that even minor changes in these processes will not cause our product candidates to perform differently and affect the results of our ongoing clinical trials, future clinical trials, or the performance of the product once commercialized. In some circumstances, changes in manufacturing operations, including to our protocols, processes, materials or

facilities used, may require us to perform additional preclinical or comparability studies, or to collect additional clinical data from patients prior to undertaking additional clinical studies or filing for regulatory approval for a product candidate. These requirements might lead to delays in our clinical development and commercialization plans for our product candidates, and might increase our development costs substantially.

Even if we were able to commercialize our products focused on rare genetic diseases, product sales of these products might not justify the cost of development.

Because of the small patient population for a rare genetic disease, if pricing is not approved or accepted in the market at an appropriate level for an approved therapeutic product with orphan drug designation, such drug may not generate enough revenue to offset costs of development, manufacturing, marketing, and commercialization despite any benefits received from the rare orphan drug designation, such as market exclusivity, assistance in clinical trial design, or a reduction in user fees or tax credits related to development expense. Furthermore, our estimates regarding potential market size for any rare genetic indication may be materially different from what we discover to exist at the time we commence commercialization, if any, for a therapeutic product, which could result in significant changes in our business plan and have a material adverse effect on our business, financial condition, results of operations, and prospects.

We face substantial competition and rapid technological change and the possibility that others may discover, develop or commercialize products before or more successfully than us.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We face competition with respect to our current product candidates and will face competition with respect to any future product candidates from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. Many of our competitors have significantly greater financial, technical and human resources. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

Our competitors may obtain marketing approval of their products more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products.

Our competitors will also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

There are numerous currently approved therapies for treating the conditions our products address and, consequently, competition in these markets is intense. Many of these approved drugs are well established therapies or products and are widely accepted by physicians, patients and third-party payors. Some of these drugs are branded and subject to patent protection and non-patent regulatory exclusivity, and others are available on a generic basis.

Insurers and other third-party payors may also encourage the use of generic products or specific branded products. We expect that any of our product candidates, if approved, would be priced at a significant premium over competitive generic, including branded generic, products, but, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. This may make it difficult for us to differentiate our product from currently approved therapies, which may adversely impact our business strategy. If we are not able to compete effectively against our current and future competitors, our business will not grow, and our financial condition and operations will suffer.

Our products might not achieve adequate market acceptance among physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if our product candidates have or receive marketing approval, they might not gain adequate market acceptance among physicians, patients and others in the medical community. Our commercial success also depends on coverage and adequate reimbursement of our product candidates by third-party payors, including government payors, generally, which may be difficult or time-consuming to obtain, may be limited in scope or might not be obtained in all jurisdictions in which we may seek to market our products. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile of our product candidates, including relative to marketed products and product candidates in development by third parties;

- prevalence and severity of any side effects of our product candidates;
- relative convenience and ease of administration of our product candidates;
- cost effectiveness of our product candidates;
- the claims we may make for our product candidates based on the approved label or any restrictions placed upon our marketing and distribution of our product candidates;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- how quickly and effectively we alone, or with a partner, can market, launch, and distribute any of our product candidates that receive marketing approval;
- the ability to commercialize any of our product candidates that receive marketing approval;
- the price of our products, including in comparison to branded or generic competitors and relative to alternative treatments;
- potential or perceived advantages of disadvantages over alternative treatments;
- the ability to collaborate with others in the development and commercialization of new products;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to establish, maintain and protect intellectual property rights related to our product candidates;
- the entry of generic versions of our products onto the market;
- the number of products in the same therapeutic class as our product candidates;
- the effect of current and future healthcare laws on our drug candidates;
- the ability to secure favorable managed care formulary positions, including federal healthcare program formularies;
- the ability to manufacture commercial quantities of any of our product candidates that receive marketing approval;
- acceptance of any of our product candidates that receive marketing approval by physicians and other healthcare providers; and
- potential post-marketing commitments imposed on regulatory authorities, such as patient registries.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, third-party payors and patients, we might not generate or derive sufficient revenue from that product candidate and might not become or remain profitable.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Given our limited resources, we have prioritized certain of our product candidates over others at our management's discretion. We have also discontinued development of certain product candidates due to results of clinical trials. We continually evaluate our capital allocation for each product candidate, and, in the future, may de-prioritize or cancel the development of certain product candidates that currently appear in our milestone chart. If the development of our product candidates is unsuccessful or, if successful but the products do not achieve an adequate level of market acceptance, we may no longer have the ability or resources to further develop any other product candidates. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications might not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Risks Related to Regulatory Approval of Our Product Candidates

The marketing approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming, costly and inherently unpredictable. Our inability to obtain regulatory approval for our product candidates would substantially harm our business.

The time required to obtain approval to market new drugs by the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any future product candidates will ever obtain regulatory approval. Moreover, the filing of an NDA or BLA for products that have not been granted ODD requires a payment of a significant application fee under the Prescription Drug User Fee Act upon submission. Any subsequent clinical data submissions to the NDA or BLA (i.e., for new indications) are also assessed an application fee. The filing of an NDA or BLA for our product candidates that do not have ODD may be delayed due to our lack of financial resources to pay such user fee.

Our product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree on the design or implementation of our clinical trials, including the methodology used in our trial, our chosen endpoints, our statistical analysis, or our proposed product indication. For instance, the FDA may find that the designs that we are utilizing in our planned clinical trial does not support an adequate and well-controlled study. The FDA also might not agree with the various disease scales and evaluation tools that we may use in our clinical trials to assess the efficacy of our product candidates. Further, the FDA might not agree with our endpoints and/or indications selected for our development programs;
- the FDA or comparable foreign regulatory authorities may disagree with our development plans for our product candidates;
- Our failure to demonstrate to the satisfaction of the FDA or comparable regulatory authorities that a product candidate is safe and effective for its proposed indication;
- Our clinical trials may fail to meet the level of statistical significance required for approval;
- We may fail to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- data collected from clinical trials of our product candidates may be insufficient to support the submission and filing of an NDA, other submission or to obtain marketing approval, and FDA may require additional studies to show that our product candidates are safe or effective;
- We may fail to obtain approval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies; or
- there may be changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or comparable foreign regulatory authority may require more information, including additional preclinical or clinical studies to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program. This lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain approval to market our product candidates, which would significantly harm our business, results of operations and prospects. In addition, even if we were to obtain approval, regulatory authorities may approve any or all of our product candidates for fewer or more limited indications than we request, may require that contraindications, warnings or precautions be included in the product labeling, including a black-box warning, may grant approval with a requirement of costly post-marketing clinical trials or other post-market requirements, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we complete the necessary clinical trials, we cannot predict when or if we will obtain marketing approval to commercialize a product candidate or the approval may be for a narrower indication than we expect.

We cannot commercialize a product candidate until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies might not complete their review processes in a timely manner, or we might not be able to obtain marketing approval from the relevant regulatory agencies.

Additional delays may result if the FDA, an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory authorities also may approve a product candidate for fewer or more limited indications than requested, may impose significant limitations in the form of narrow indications, warnings, including black-box warnings, precautions or contra-indications with respect to conditions of use or may grant approval subject to the performance of costly post-marketing clinical trials or other post-marketing requirements, including a REMS. In addition, regulatory agencies might not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Our drugs, if approved, may be required to carry warnings comparable to this and other class-wide warnings. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we were to obtain approval for our product candidates with the Rare Pediatric Disease Designation, the Rare Pediatric Disease Priority Review Voucher Program may no longer be in effect at the time of such approval or we might not be able to capture the value of the Rare Pediatric Disease Priority Review Voucher Program.

RPDD is granted by the FDA in the case of serious or life-threatening diseases affecting fewer than 200,000 people in the United States in which the serious or life-threatening manifestations are primarily in individuals 18 years of age and younger. Upon request, the FDA has the authority to grant a Rare Pediatric Disease PRV for drug and biologic applications approved to prevent or treat a rare pediatric disease and deemed eligible for priority review, among other criteria.

The Consolidated Appropriations Act, 2021 was signed into law on December 27, 2020. As part of this legislation, the FDA Rare Pediatric Disease Designation Program has been extended through 2024, permitting the issuance of PRVs through September 30, 2024 for drugs and biologics receiving FDA approval before September 30, 2026. AVTX-006, AVTX-801, AVTX-802 and AVTX-803 are each potentially eligible for a PRV upon FDA approval of each drug, but there is no guarantee that a voucher(s) will be granted. Moreover, any PRV may be sold or transferred an unlimited number of times. Although PRVs may be sold or transferred to third parties, there is no guarantee that we will be able to realize any value if we receive and were to sell a PRV.

We may pursue government funding for products we are developing, including those we are developing for the treatment of COVID-19 ARDS. If we do not apply for or are unable to obtain such government funding, we might be unable to develop certain product candidate.

While we have not yet received U.S. government funding, we may apply to receive funding from the U.S. government for products we are developing, including those we are developing for the treatment of COVID-19 ARDS. If applied for and granted, the government funding could be instrumental to certain product developments. However, there can be no assurances that we will apply for such government funding, or that if we do apply, we will receive such government funding. If we do not receive government funding, we might not be able to develop certain products, which could adversely impact our business, financial condition and results of operations.

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

Even if we obtain marketing approval for a product candidate, we would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and annual reporting of safety and other post-market information. The FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may withdraw approval, require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. In addition, any marketing approvals that we obtain for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval or contain requirements for potentially costly post-marketing testing and other requirements, including Phase 4 clinical trials, imposition of a REMS and surveillance to monitor the safety and efficacy of the product candidate.

In addition, manufacturers of drug products and their facilities, including contracted facilities, are subject to periodic inspections by the FDA and other regulatory authorities for compliance with GMP regulations and standards. If we or a regulatory agency discover previously unknown problems with the facility where the product is manufactured, we may be subject to reporting obligations and a

regulatory agency may impose restrictions on that product, the manufacturing facility, us, or our suppliers, including requesting recalls or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates, our contractors, the manufacturing facilities for our product candidates or others working on our behalf fail to comply with applicable regulatory requirements, either before or after marketing approval, a regulatory agency may:

- issue Warning Letters, Untitled Letters, or Form 483s, all of which document compliance issues identified by FDA;
- mandate modifications to promotional materials or labeling, or require us to provide corrective information to healthcare practitioners;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines, restitution or disgorgement, as well as imprisonment;
- suspend or withdraw marketing approval;
- suspend or terminate any ongoing clinical studies;
- refuse to approve pending applications or supplements to applications filed by us;
- debar us from submitting marketing applications, exclude us from participation in federal healthcare programs, require a corporate integrity agreement or deferred prosecution agreements, debar us from government contracts and refuse future orders under existing contracts;
- suspend or impose restrictions on operations, including restrictions on marketing, distribution or manufacturing of the product, or the imposition of costly new manufacturing requirements or use of alternative suppliers; or
- seize or detain products, refuse to permit the import or export of products, or request that we initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to continue our development programs, commercialize our products and generate revenue.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, the Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress and the public. While the FDA does not restrict physicians from prescribing approved drugs for uses outside of the drugs' approved labeling, known as off-label use, pharmaceutical manufacturers are strictly prohibited from promoting and marketing their products for such uses. Violations, including promotion of our products for off-label uses, are subject to enforcement letters, inquiries, investigations, civil and criminal sanctions by the government, corporate integrity agreements, deferred prosecution agreements, debarment from government contracts and refusal of future orders under existing contracts, and exclusion from participation in federal healthcare programs. Additionally, comparable foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States.

In the United States, engaging in the impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines, debarment from government contracts and refusal of future orders under existing contracts, deferred prosecution agreements, and corporate integrity agreements with governmental authorities that materially restrict the manner in which a company promotes or distributes drug products. These false claims statutes include the federal civil False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government decides to intervene and prevails in the lawsuit, the individual will share in any fines or settlement funds. If the government does not intervene, the individual may proceed on his or her own. Since 2004, these False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements, such as settlements regarding certain sales practices promoting off-label drug uses involving fines that are as much as $3 billion. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations and prospects.

The FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay marketing approval, and the sale and promotion of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If we are unable to obtain, or are delayed in obtaining, state regulatory licenses for the distribution of our products, we would not be able to sell our product candidates in such states.

The majority of states require manufacturer and/or wholesaler licenses for the sale and distribution of drugs into that state. The application process is complicated, time consuming, costly and requires dedicated personnel or a third party to oversee and manage. If we are delayed in obtaining these state licenses, or denied the licenses, even with FDA approval, we would not be able to sell or ship product into that state which would adversely affect our sales and revenues.

We have chosen, and we may in the future choose, to conduct clinical trials for certain of our product candidates at sites outside the United States, and the FDA might not accept data from trials conducted in such locations.

We have chosen, and we may in the future choose, to conduct one or more of our clinical trials outside the United States. We currently are conducting trials for the development of AVTX-007 for the treatment of AOSD in Ukraine, Poland, and Belgium. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical trials conducted outside of the United States must be representative of the population for whom we intend to seek approval in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any of our clinical trials that we determine to conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of the product candidate. These clinical trials outside of the United States might also be subject to delays and risks surrounding geopolitical events, such as the current conflict in Ukraine.

Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates outside the United States, which would limit our market opportunities and adversely affect our business.

In order to market and sell our products in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country might not be accepted by regulatory authorities in other countries. If we fail to comply with the regulatory requirements in international markets and receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected. We might not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. Approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. Also, regulatory approval for any of our product candidates may be withdrawn. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval in another jurisdiction. Our failure to obtain approval of any of our product candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that product candidate and our business prospects could decline.

Risks Related to the Commercialization of Our Product Candidates

We might not be successful in our efforts to develop and commercialize our product candidates.

Our continued development of our preclinical product candidates will be dependent on receiving positive data that, in our judgment, merits advancing such programs. Even if we are successful in continuing to build and expand our pipeline, the potential product candidates that we identify might not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. Similarly, even if the FDA accepts our INDs, there is no guarantee that we will be successful in our efforts to advance our preclinical product candidates into clinical trials.

Once commercialized, some of our products may face significant competition from non-prescription competition and consumer substitution, and our operating results will suffer if we fail to compete effectively.

We may be subject to non-prescription competition and consumer substitution for certain of our pipeline assets. For example, the therapies in our rare genetic disease pipeline, AVTX-801, AVTX-802 and AVTX-803, are ultra-pure formulations of D-galactose, D-mannose and L-fucose, respectively. These formulations are naturally occurring substances contained in various foods, including dairy products and fruit. Additionally, D-galactose and D-mannose are also marketed by others as non-prescription dietary supplements. Once approved by the FDA and commercially available, we cannot be sure physicians will view the pharmaceutical grade purity and tested safety of AVTX-801, AVTX-802 or AVTX-803 as having a superior therapeutic profile to the naturally occurring formulations and dietary supplements. In addition, to the extent the net price of AVTX-801, AVTX-802 or AVTX-803, after insurance and offered discounts, is significantly higher than the prices of commercially available formulations marketed by other companies as dietary supplements (through that lack of coverage by insurers or otherwise), physicians and pharmacists may recommend these commercial alternatives instead of writing or filling prescriptions for AVTX-801, AVTX-802 or AVTX-803, or patients may elect on their own to take commercially available supplements. Either of these outcomes may adversely impact our results of operations by limiting how we price our product and limiting the revenue we receive from the sale of AVTX-801, AVTX-802 and AVTX-803 due to reduced market acceptance.

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If any of our product candidates are approved for commercialization, we may enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for approval of drugs in foreign countries;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- foreign reimbursement, pricing and insurance regimes;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- foreign taxes;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

These and other risks associated with our international operations may materially adversely affect our ability to attain or maintain profitable operations.

Even if we commercialize any of our product candidates, these products may become subject to unfavorable third-party coverage and reimbursement policies, healthcare reform initiatives, or pricing regulations, any of which could negatively impact our business.

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products will be available from government authorities, private health insurers, health maintenance organizations and other entities. These third-party payors determine which medications they will cover and establish reimbursement levels, and increasingly attempt to control costs by limiting coverage and the amount of reimbursement for particular medications. Several third-party payors are requiring that drug companies provide them with predetermined discounts from list prices, are using preferred drug lists to leverage greater discounts in competitive classes and are challenging the prices charged for drugs. In addition, federal programs impose penalties on drug manufacturers in the form of mandatory additional rebates and/or discounts if commercial prices increase at a rate greater than the Consumer Price Index-Urban, and these rebates and/or discounts, which can be substantial, may impact our ability to raise commercial prices. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if coverage is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or available only to limited levels, we might not successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates for a drug may vary according to the clinical setting in which it is used and may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Prices paid for a drug also vary depending on the class of trade. Prices charged to government customers are subject to price controls and private institutions obtain discounts through group purchasing organizations. Net prices for drugs may be further reduced by mandatory discounts or rebates required by government healthcare programs and demanded by private payors, and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Moreover, the regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates even if our product candidates obtain marketing approval.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and related to the commercial sale of our products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. For example, we may be sued if any product we sell allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against claims that our product candidates or products that we may develop caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial subjects or patients;
- loss of revenue;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- diversion of management and scientific resources from our business operations;

- the inability to commercialize any products that we may develop; and
- a decline in our stock price.

We currently hold product and clinical trial liability insurance coverage, but it might not adequately cover all liabilities that we incur. We might not be able to maintain clinical trial insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. We also maintain insurance coverage for our commercially available products, which might not adequately cover all liabilities that we may incur. We might not be able to maintain insurance coverage for our approved products at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A product liability claim or series of claims brought against us, whether or not successful, but particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our reputation and business.

If, in the future, we are unable to grow our own sales, or establish marketing and distribution capabilities or enter into licensing or collaboration agreements for these purposes, we might not be successful in commercializing our product candidates.

We do not currently have a robust sales or marketing infrastructure. To develop our internal sales, distribution and marketing capabilities for new product candidates, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any new product candidates will be approved. For product candidates for which we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- Our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- inability of marketing personnel to develop effective marketing materials;
- the inability of sales personnel to obtain access to physicians or educate adequate numbers of physicians on the clinical benefits of our products to achieve market acceptance;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the costs associated with training sales personnel on legal compliance matters and monitoring their actions;
- liability for sales personnel failing to comply with the applicable legal requirements; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Where and when appropriate, we may elect to utilize contract sales forces or strategic partners to assist in the commercialization of our product candidates. If we enter into arrangements with third parties to perform sales, marketing and distribution services for our products, the resulting revenues or the profitability from these revenues to us are likely to be lower than if we had sold, marketed and distributed our products ourselves. In addition, we might not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively. Such third parties may also not comply with the applicable regulatory requirements, which could potentially expose us to regulatory and legal enforcement actions.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct, supervise and monitor our clinical trials. The failure of these third parties to successfully carry out their contractual duties or meet expected deadlines could substantially harm our business because we might not obtain marketing approval for or commercialize our product candidates in a timely manner or at all.

We rely upon third-party CROs to monitor and manage data for our clinical programs. We rely on these parties for execution of our clinical trials and, while we have agreements governing their activities, we have limited influence over their actual performance and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We, our clinical trial sites, and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we, any of our CROs or clinical trial sites fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications, if at all. In addition, we are required to report certain financial interests of our third-party investigators if these relationships exceed certain financial thresholds or meet other criteria. The FDA or comparable foreign regulatory authorities may question the integrity of the data from those clinical trials conducted by principal investigators who previously served or currently serve as scientific advisors or consultants to us from time to time and receive cash compensation in connection with such services or otherwise receive compensation from us that could be deemed to impact study outcome, proprietary interests in a product candidate, certain company equity interests, or significant payments of other sorts. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements. In addition, we must conduct our clinical trials with product produced under applicable GMP requirements. Failure to comply with these regulations may require us to repeat preclinical and clinical trials, which would delay the marketing approval process.

Our CROs and clinical trial sites are not our employees, and, except for remedies available to us under our agreements with such CROs and clinical trial sites, we cannot control whether or not they devote sufficient time and resources to our ongoing clinical, nonclinical and preclinical programs. These CROs and clinical trial sites may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If CROs or clinical trial sites do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we might not be able to obtain marketing approval for or successfully commercialize our product candidates or we may be subject to regulatory enforcement actions. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. To the extent we are unable to successfully identify and manage the performance of third-party service providers in the future, our business may be adversely affected.

Switching or adding CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, prospects, financial condition and results of operations.

We use third parties to manufacture all of our product candidates. This may increase the risk that we will not have sufficient quantities of our product candidates to conduct our clinical trials or such quantities at an acceptable cost, which could result in the delay, prevention, or impairment of clinical development and commercialization of our product candidates.

We do not own or operate, and have no plans to establish, any manufacturing facilities for our product candidates. We have limited personnel with experience in drug manufacturing and we lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale.

We currently outsource all manufacturing of our product candidates to third parties typically without any guarantee that there will be sufficient supplies to fulfill our requirements or that we may obtain such supplies on acceptable terms. Any delays in obtaining adequate supplies with respect to our product candidates may delay the development or commercialization of our other product candidates.

In addition, we do not currently have agreements with all third-party manufacturers for the long-term commercial supply of our product candidates. We may be unable to enter agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms. Even if we enter into these agreements, the various manufacturers of each product candidate will likely be single source suppliers to us for a significant period of time.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA or BLA to the FDA. While we are ultimately responsible for the manufacture of our product candidates, other than through our contractual arrangements, we do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with GMP requirements for manufacture of both active drug substances and finished drug products for clinical supply and eventually for commercial supply, if we receive regulatory approval. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, we will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. Failure of our contract manufacturers to comply with the applicable regulatory requirements may also subject us to regulatory enforcement actions. In addition, other than through our contractual agreements, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved.

Reliance on third-party manufacturers subjects us to risks that would not affect us if we manufactured the product candidates ourselves, including:

- reliance on the third parties for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreements by the third parties because of factors beyond our control;
- the possible misappropriation of our proprietary information, including trade secrets and know-how;
- the possibility of termination or nonrenewal of the agreements by the third parties because of our breach of the manufacturing agreement or based on our own business priorities;
- the disruption and costs associated with changing suppliers, including additional regulatory filings;
- failure to satisfy our contractual duties or obligations;
- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and/or product quality issues related to manufacturing development and scale-up;
- costs and validation of new equipment and facilities required for scale-up;
- failure to comply with applicable laws, regulations, and standards, including cGMP and similar foreign standards;
- deficient or improper record-keeping;
- contractual restrictions on our ability to engage additional or alternative manufacturers;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates or any future product candidate in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- lack of access or licenses to proprietary manufacturing methods used by third-party manufacturers to make our product candidates;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or regulatory sanctions related to the manufacture of our or other company's products;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our products under specified storage conditions and in a timely manner.

Our product candidates may compete with other products and product candidates for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that are both capable of manufacturing for us and willing to do so. The COVID-19 pandemic has also limited the available capacity of these manufacturers due to staffing shortages, production slowdowns or stoppages because of overall increased manufacturing in the biotechnology industry, and manufacturers' obligations to manufacture and distribute vaccines to address the spread of COVID-19, among other things. In addition, the manufacture of biologics requires significant expertise, including the development of advanced manufacturing techniques and process controls. The process is highly complex and we may encounter difficulties in production. These issues may include difficulties with production costs, production yields and quality control, including stability of the product candidate.

Further, our product candidates may require new or specialized manufacturing with limited third-party manufacturers available to provide these services. The occurrence of any of these problems could significantly delay our clinical trials or the commercial availability of our product candidates. If our existing third-party manufacturers, or the third parties that we engage in the future to manufacture a product for commercial sale or for our clinical trials, should cease to continue to do so for any reason, we likely would experience delays in obtaining sufficient quantities of our product candidates for us to meet commercial demand or to advance our clinical trials while we identify and qualify replacement suppliers. If for any reason we are unable to obtain adequate supplies of our product candidates or the drug substances used to manufacture them, it will be more difficult for us to develop our product candidates and compete effectively.

Our suppliers are subject to regulatory requirements, covering manufacturing, testing, quality control, manufacturing, and record keeping relating to our product candidates, and subject to ongoing inspections by the regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing capacity while we seek to secure another supplier that meets all regulatory requirements, as well as market disruption related to any necessary recalls or other corrective actions.

We might not succeed in establishing and maintaining development collaborations, which could adversely affect our ability to develop and commercialize product candidates.

A part of our strategy is to enter into product development collaborations in the future, including collaborations with major biotechnology or pharmaceutical companies for the development or commercialization of our current and future product candidates. We also face significant competition in seeking appropriate development partners and the negotiation process is time-consuming and complex. We might not succeed in our efforts to establish development collaborations or other alternative arrangements for any of our existing or future product candidates and programs because our research and development pipeline may be insufficient, our product candidates and programs may be deemed to be at too early a stage of development for collaborative effort and/or third parties might not view our product candidates and programs as having the requisite potential to demonstrate safety and efficacy.

Furthermore, any collaborations that we enter into might not be successful. The success of our development collaborations will depend heavily on the efforts and activities of our collaborators. Furthermore, any collaborations that we enter into might not be successful. The success of our development collaborations will depend heavily on the efforts and activities of our collaborators. Our relationship with any future collaborations may pose several risks, including the following:

- collaborators have significant discretion in determining the amount and timing of the efforts and resources that they will apply to these collaborations;
- collaborators might not perform their obligations as expected;
- the nonclinical studies and clinical trials conducted as part of these collaborations might not be successful;
- collaborators might not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on nonclinical study or clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay nonclinical studies and clinical trials, provide insufficient funding for nonclinical studies and clinical trials, stop a nonclinical study or clinical trial or abandon a product candidate, repeat or conduct new nonclinical studies or clinical trials or require a new formulation of a product candidate for nonclinical studies or clinical trials;
- We might not have access to, or may be restricted from disclosing, certain information regarding product candidates being developed or commercialized under a collaboration and, consequently, may have limited ability to inform our stockholders about the status of such product candidates;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates developed in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval might not commit sufficient resources to the marketing and distribution of any such product candidate;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development of any product candidates, may cause delays or termination of the research, development or commercialization of such product candidates, may lead to additional responsibilities for us with respect to such product candidates or may result in litigation or arbitration, any of which would be time consuming and expensive;

- collaborators might not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- disputes may arise with respect to the ownership or inventorship of intellectual property developed pursuant to our collaborations;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- the terms of our collaboration agreement may restrict us from entering into certain relationships with other third parties, thereby limiting our options; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Even if we are successful in our efforts to establish development collaborations, the terms that we agree upon might not be favorable to us and we might not be able to maintain such development collaborations 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 collaboration 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. Additionally, collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

If we fail to establish and maintain additional development collaborations related to our product candidates:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly and we may need to seek additional financing, which might not be available on favorable terms, or at all;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted;
- we will bear all of the risk related to the development of any such product candidates;
- we may have to expend unexpected efforts and funds if we are unable to obtain the results of third-party clinical trials; and
- the competitiveness of any product candidate that is commercialized could be reduced.

Risks Related to Intellectual Property

As appropriate, we intend to seek all available periods of regulatory exclusivity for our product candidates. However, there is no guarantee that we will be granted these periods of regulatory exclusivity or that we will be able to maintain these periods of exclusivity.

The FDA grants product sponsors certain periods of regulatory exclusivity, during which the agency might not approve, and in certain instances, might not accept, certain marketing applications for competing drugs. For example, product sponsors may be eligible for five years of exclusivity from the date of approval of a new chemical entity, seven years of exclusivity for drugs that are designated to be orphan drugs, and/or a six-month period of exclusivity added to any existing exclusivity period or patent life for the submission of FDA requested pediatric data. While we intend to apply for all periods of market exclusivity that we may be eligible for, there is no guarantee that we will receive all such periods of market exclusivity. Additionally, under certain circumstances, the FDA may revoke the period of market exclusivity. As a result, there is no guarantee that we will be able to maintain a period of market exclusivity, even if granted. In the case of ODD, other benefits, such as tax credits and exemption from user fees may be available. If we are not able to obtain or maintain orphan drug designation or any period of market exclusivity to which we may be entitled, we will be materially harmed, as we will potentially be subject to greater market competition and may lose the benefits associated with programs.

If we are unable to obtain or maintain intellectual property rights, or if the scope of patent protection is not sufficiently broad, competitors could develop and commercialize products similar or identical to ours, and we might not be able to compete effectively in our market.

Our success depends in significant part on our and our licensors', licensees' or collaborators' ability to establish, maintain and protect patents and other intellectual property rights and operate without infringing the intellectual property rights of others. We have filed numerous patent applications both in the United States and in foreign jurisdictions to obtain patent rights to inventions we have discovered. We have also licensed from third parties' rights to patent portfolios.

The patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees or collaborators might not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Moreover, in some circumstances, we might not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from or license to third parties and are reliant on our licensors, licensees or collaborators. Therefore, these patents and applications might not be prosecuted and enforced in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our licensors', licensees' or collaborators' pending and future patent applications might not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our licensors, licensees or collaborators to narrow the scope of the claims of our or our licensors', licensees' or collaborators' pending and future patent applications, which may limit the scope of patent protection that may be obtained. Our and our licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications, and then only to the extent the issued claims cover the technology.

Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio might not provide us with sufficient rights to exclude others from commercializing products similar or identical to our products. We expect to seek extensions of patent terms where these are available in any countries where we are prosecuting patents. This includes in the United States under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent term extension of up to five years beyond the expiration of the patent. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, might not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited

extensions than we request. If this occurs, our competitors may take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

If we breach the license and development agreements related to our product candidates, we could lose the ability to develop and commercialize our product candidates.

Our commercial success depends upon our ability, and the ability of our licensors and collaborators, to develop, manufacture, market and sell our product candidates and use our and our licensors' or collaborators' proprietary technologies without infringing the proprietary rights of third parties. If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose the ability to continue the development and commercialization of our product candidates or face other penalties under these agreements. We are party to the following agreements:

- the KKC License Agreement;
- an exclusive global license with MedImmune Limited, a subsidiary of AstraZeneca, to develop and commercialize AVTX-007 (the "AZ License Agreement");
- an exclusive license agreement with Sanford Burnham Prebys Medical Discovery Institute to a portfolio of issued patents and patent applications covering an immune checkpoint program, which we refer to as AVTX-008 (the "SBP License Agreement");
- an Exclusive License Agreement with OSI Pharmaceuticals, LLC, an indirect wholly owned subsidiary of Astellas, for the worldwide development and commercialization of AVTX-006 (the "Astellas License Agreement"); and
- exclusive license agreements with Merck & Co., Inc. and its affiliates for the compounds used in AVTX-301 and the COMTi platform, including AVTX-406. In 2021, we out-licensed our rights in respect of AVTX-301 and assigned our rights, title, interest and obligations of AVTX-406.

If we fail to comply with the obligations under these agreements, including payment terms, our licensors may have the right to terminate any of these agreements, in which event we might not be able to develop, market or sell the relevant product candidate. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in us having to negotiate new or reinstated agreements, which might not be available to us on equally favorable terms, or at all, or cause us to lose our rights under these agreements, including our rights to intellectual property or technology important to our development programs. Any of these occurrences may harm our business, financial condition and prospects significantly.

We may be required to make significant payments in connection with our license and development agreements.

We are party to license and development agreements with various third parties. For example, we are party to the KKC License Agreement, the Astellas License Agreement, the AZ License Agreement, and the SBP License Agreement. We may be required to make significant payments in connection with such agreements including (but not limited to):

- Under the KKC License Agreement, we will incur development costs for AVTX-002 and are required to make significant payments in connection with the achievement of specified development and regulatory milestones. Additionally, upon commercialization, we are obligated to pay KKC sales-based milestones and royalties;
- As a result of our exercise of the option granted under the AZ Agreement, we might incur development costs for AVTX-006 and might be required to make significant payments in connection with the achievement of certain development and regulatory milestones. Upon commercialization, we are required to pay sales-based milestones and royalties; and
- Under the Astellas Agreement, we will incur development costs for AVTX-007 and are required to make significant payments in connection with the achievement of certain development and regulatory milestones. Upon commercialization, we are required to pay sales-based milestones and royalties.

If the obligations become due under the terms any of these agreements, we might not have sufficient funds available to meet our obligations and our development efforts may be negatively impacted.

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

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO, and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our licensors or collaborators fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Third parties may initiate legal proceedings against us alleging that we infringed their intellectual property rights, or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Third parties may initiate legal proceedings against us or our licensors or collaborators alleging that we or our licensors or collaborators infringe their intellectual property rights or we or our licensors or collaborators may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, reexaminations, inter partes reviews or derivation proceedings before the United States or other jurisdictions. These proceedings can be expensive and time-consuming and many of our or our licensors' or collaborators' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors or collaborators can.

An unfavorable outcome could require us or our licensors or collaborators to cease using the related technology or developing or commercializing our product candidates, 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 or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business.

Third parties may infringe on our or our licensors' or collaborators' patents or misappropriate or otherwise violate our or our licensors' or collaborators' intellectual property rights. In the future, we or our licensors or collaborators may initiate legal proceedings to enforce or defend our or our licensors' or collaborators' intellectual property rights, to protect our or our licensors' or collaborators' trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us or our licensors or collaborators to challenge the validity or scope of intellectual property rights we own or control. The proceedings can be expensive and time-consuming and many of our or our licensors' or collaborators' adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our licensors or collaborators can. Accordingly, despite our or our licensors' or collaborators' efforts, we or our licensors or collaborators might not prevent third parties from infringing upon or misappropriating intellectual property rights we own or control, particularly in countries where the laws might not protect those rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that we or our licensors' or collaborators' patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our or our licensors' or collaborators' patents at risk of being invalidated, held unenforceable or interpreted narrowly.

Third party pre-issuance submission of prior art to the USPTO, or opposition, derivation, reexamination, inter partes review or interference proceedings, or other pre-issuance or post-grant proceedings in the United States or other jurisdictions provoked by third parties or brought by us or our licensors or collaborators may be necessary to determine the priority of inventions with respect to our

or our licensors' or collaborators' patents or patent applications. An unfavorable outcome could require us or our licensors or collaborators to cease using the related technology and commercializing our product candidates, 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 or our licensors or collaborators a license on commercially reasonable terms or at all. Even if we or our licensors or collaborators obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our licensors or collaborators. In addition, if the breadth or strength of protection provided by our or our licensors' or collaborators' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and it may distract our management and other employees. We could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent.

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 warrants or shares of our common stock.

Our inability to protect our confidential information and trade secrets would harm our business and competitive position.

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. Though we seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties, as well as by entering into confidentiality and invention or patent assignment agreements with our employees and consultants, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we might not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect trade secrets. If a competitor lawfully and without breach of a confidentiality obligation obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Changes in 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 biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time-consuming, and inherently uncertain. The United States 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 and our licensors' or collaborators' 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 Congress, the federal courts, and the USPTO the laws and regulations governing patents could change in unpredictable ways that would weaken our and our licensors' or collaborators' ability to obtain new patents or to enforce existing patents and patents we and our licensors or collaborators may obtain in the future. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our and our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents. On September 16, 2011, the America Invents Act was signed into law. The America Invents Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO also developed regulations and procedures to govern administration of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and in particular, the first to file provisions, only became effective on March 16, 2013. The America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our licensors' or collaborators' patent applications and the enforcement or defense of our or our licensors' or collaborators' issued patents, all of which could have a material adverse effect on our business and financial condition.

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

Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our or our licensors' or collaborators' intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual

property rights to the same extent as federal and state laws in the United States. Consequently, we and our licensors or collaborators might not be able to prevent third parties from practicing our and our licensors' or collaborators' inventions in all countries outside the United States, or from selling or importing products made using our and our licensors' or collaborators' inventions in and into the United States or other jurisdictions. Competitors may use our and our licensors' or collaborators' 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 and our licensors or collaborators have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and our and our licensors' or collaborators' patents or other intellectual property rights might 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 and our licensors or collaborators to stop the infringement of our and our licensors' or collaborators' patents or marketing of competing products in violation of our and our licensors' or collaborators' proprietary rights generally. Proceedings to enforce our and our licensors' or collaborators' patent rights in foreign jurisdictions could result in substantial costs and divert our and our licensors' or collaborators' efforts and attention from other aspects of our business, could put our and our licensors' or collaborators' patents at risk of being invalidated or interpreted narrowly and our and our licensors' or collaborators' patent applications at risk of not issuing and could provoke third parties to assert claims against us or our licensors or collaborators. We or our licensors or collaborators might not prevail in any lawsuits that we or our licensors or collaborators initiate and the damages or other remedies awarded, if any, might not be commercially meaningful.

The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' or collaborators' patents, requiring us or our licensors or collaborators to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch biosimilar versions of our products. Certain countries, including India and China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors or collaborators may have limited remedies if patents are infringed or if we or our licensors or collaborators are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' or collaborators' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Risks Related to Legal Compliance

Ongoing changes to healthcare laws and regulations may increase the difficulty and cost associated with commercializing our products and may affect the prices we are paid for those products.

The Healthcare sector is heavily regulated in the United States and abroad, and new laws, regulations, and/or judicial decisions—or new interpretations of such laws, regulations, or decisions—could negatively impact our business, operations, and financial condition. Our business and financial operations could also be negatively affected by ongoing changes in health care spending policies in the United States and abroad. The United States federal government, state governments, and foreign governments have shown significant and increasing interest in cost-containment initiatives intended to limit the growth of healthcare costs, including without limitation price controls, restrictions on reimbursement, requirements for substitution of generic products for branded prescription drugs, prior authorization requirements, and increased copays and cost shares for beneficiaries. The Patient Protection and Affordable Care Act ("Affordable Care Act"), for instance, increased federal oversight of private health insurance plans and included a number of provisions designed to reduce Medicare expenditures and the cost of health care generally, to reduce fraud and abuse, and to provide access to increased health coverage. The implemented provisions of the Affordable Care Act that are of importance to the commercialization of our product and product candidates, if approved, include:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs or biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the U.S. civil False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- 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;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- requirements to report certain financial arrangements with physicians and teaching hospitals;
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Efforts to reform the healthcare sector are ongoing. Since its enactment, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the Affordable Care Act. For example, the TCJA repealed the Affordable Care Act's "individual mandate." The repeal of this provision of the Affordable Care Act, which required most Americans to carry a minimal level of health insurance, became effective in 2019. It is unclear what impact the repeal of the individual mandate will have on the viability of the insurance marketplaces established under the Affordable Care Act or on the need for future reforms. The Trump administration also took executive actions to delay implementation of portions of the Affordable Care Act, including directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. Further, the BBA of 2018, among other things, amended the Affordable Care Act to increase 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." These revisions became effective January 1, 2019.

The Biden administration has signaled that it plans to build on the Affordable Care Act and to expand the number of people who are presently eligible for subsidies under the law. On January 28, 2021, President Biden issued a new Executive Order directing federal agencies to reconsider rules and other policies that limit Americans' access to health care and to consider actions that will protect and strengthen that access. Under this Executive Order, federal agencies are directed to re-examine: policies that undermine protections for

people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the Affordable Care Act that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the Affordable Care Act; and policies that reduce affordability of coverage or financial assistance, including for dependents.

We expect further reform to the Affordable Care Act, to the Medicare and Medicaid programs, and to the regulation of the healthcare sector generally. Some of these changes could have a material adverse effect on our business and operations. Ongoing and future healthcare reform measures may result, for instance, in more rigorous coverage criteria and in additional downward pressure on the price that we receive for our product and product candidates, if approved, and could seriously harm our future revenues. The prices of prescription drugs have been the subject of considerable discussion and debate in the United States and abroad. There have been several recent U.S. congressional inquiries into prescription drug pricing, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare, and reform government program reimbursement methodologies for products. Any reduction in reimbursement from Medicare, Medicaid, or other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain and maintain profitability of our product and product candidates, if approved.

Legislative efforts at cost containment in healthcare programs are ongoing. The Budget Control Act of 2011, for instance, created, among other things, 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 in funding to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2029 unless additional Congressional action is taken. The CARES Act suspended the 2% Medicare sequester from May 1, 2020 through December 31, 2020—and also extended the sequester by one year, through 2030. The American Taxpayer Relief Act of 2012 also reduced Medicare payments to certain providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws, and others, may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

At the state level, individual states are increasingly aggressive in 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. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug formularies and other health care programs. These measures could reduce the ultimate demand for our product and potential products, if approved, and/or may constrain the prices that we are able to charge for such products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Our relationships with commercial and government customers, healthcare providers, third-party payors, and others are subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare related laws, regulations and requirements, which could expose us to criminal and civil liability, exclusion from participation in federal healthcare programs, contractual damages and consequences, reputational harm, administrative burdens, and diminished profits and future earnings.

Our business and our relationships with customers, physicians, and third-party payors are subject, directly and indirectly, to federal and state health care fraud and abuse laws and regulations. These laws also apply to the physicians and third-party payors who play a primary role in the recommendation and prescription of our commercially available products. These laws may constrain the business or financial arrangements and relationships through which we market, sell, and distribute our products and will impact, among other things, our proposed sales, marketing and educational programs. There are also laws, regulations, and requirements applicable to the award and performance of federal grants and contracts.

Actions resulting in violations of these laws regulations, and requirements may result in civil and criminal liability, damages and restitution, as well as exclusion from participation in federal healthcare programs, corporate integrity agreements, deferred prosecution agreements, debarment from government contracts and grants and refusal of future orders under existing contracts or contractual damages, reputational damage, and other consequences. Restrictions under applicable federal and state healthcare related laws and regulations include but are not limited to the following:

- the federal Anti-Kickback Statute, which prohibits persons from, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for the furnishing or arranging for the furnishing, or the purchase, lease or order, or arranging for or recommending purchase, lease or order, of any good or service for which payment may be made under a federal healthcare program;
- the civil federal False Claims Act, which imposes civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; knowingly making, using or causing to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the government; conspiring to defraud the government by getting a false or fraudulent claim paid or approved by the government; or knowingly making, using or causing to be made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the criminal federal False Claims Act, which imposes criminal fines or imprisonment against individuals or entities who willfully make or present a claim to the government knowing such claim to be false, fictitious or fraudulent;
- the Veterans Health Care Act, which requires manufacturers of covered drugs to offer them for sale on the Federal Supply Schedule and requires compliance with applicable federal procurement laws and regulations;
- HIPAA, which imposes obligations on certain covered entity health care providers, health plans, and health care clearinghouses as well as their business associates that perform certain services involving individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, as well as directly applicable privacy and security standards and requirements; HIPAA also imposes criminal liability for, among other actions, knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, or knowingly and willfully making false statements relating to healthcare matters;
- the civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;
- federal transparency laws, including the federal Physician Sunshine Act (PSA) created under Section 6002 of the Affordable Care Act and its implementing regulations. The PSA requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the Centers for Medicare and Medicaid Services, or CMS, information related to payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members;
- the FCPA, which prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations; and
- analogous or similar state, federal, and foreign laws, regulations, and requirements—such as state anti-kickback and false claims laws—which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign 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; laws, regulations, and requirements applicable to the award and performance of federal contracts and grants and state, federal and foreign laws that govern the privacy and security of health and other information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations involve substantial costs. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is

possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other laws. regulations or other requirements that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, restitution exclusion from government funded healthcare programs, corporate integrity agreements, deferred prosecution agreements, debarment from government contracts and grants and refusal of future orders under existing contracts, contractual damages, the curtailment or restructuring of our operations and other consequences. If any of the physicians or other healthcare providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Moreover, availability of any federal grant funds which we may receive or for which we may apply is subject to federal appropriations law. Such grant funding may also be withdrawn or denied due to a violation of the above laws and/or for other reasons.

Failure to obtain or maintain orphan product exclusivity for any of the product candidates for which we seek this status could limit our commercial opportunity.

Regulatory authorities in the United States may designate drugs for relatively small patient populations as orphan drugs. While certain of our product candidates have received orphan drug designation, there is no guarantee that we will be able to receive such designations in the future. The FDA may grant orphan designation to multiple sponsors for the same compound or active molecule and for the same indication. If another sponsor receives FDA approval for such product before we do, we would be prevented from launching our product in the United States for the orphan indication for a period of at least seven years unless we can demonstrate clinical superiority.

Moreover, while orphan drug designation neither shortens the development or regulatory review time, nor gives the product candidate advantages in the regulatory review or approval process, generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the relevant indication, the product is entitled to a period of market exclusivity, which precludes the FDA from approving another marketing application for the same drug for the same indication for that period. The FDA, however, may subsequently approve a similar drug (or, in the U.S., the same drug) for the same indication during the first product's market exclusivity period if the FDA concludes that the later drug is shown to be safer or more effective or makes a major contribution to patient care. Orphan exclusivity in the United States also does not prevent the FDA from approving another product that is considered to be the same as our product candidates for a different indication or a different product for the same orphan indication. If another product that is the same as ours is approved for a different indication, it is possible that third-party payors will reimburse for products off-label even if not indicated for the orphan condition.

Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective, or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition or if the incidence and prevalence of patients who are eligible to receive the drug in these markets materially increase. The inability to obtain or failure to maintain adequate product exclusivity for our product candidates could have a material adverse effect on our business prospects, results of operations and financial condition.

Additionally, regulatory criteria with respect to orphan products is evolving, especially in the area of gene therapy. By example, in the United States, whether two gene therapies are considered to be the same for the purpose of determining clinical superiority (i.e., is safer, more effective, and/or makes a major contribution to patient care) depends on a number of factors, including the expressed transgene, the vector, and other features of the molecule or compound. Accordingly, whether any of our products or product candidates will be deemed to be the same as another product or product candidate is uncertain.

Our business and operations could suffer in the event of computer system failures, cyber-attacks or deficiencies in our cyber-security.

In the ordinary course of our business, we collect and store sensitive data, including intellectual property, research data, our proprietary business information and that of our suppliers, technical information about our products, clinical trial plans and employee records. Similarly, our third-party providers possess certain of our sensitive data and confidential information. The secure maintenance of this information is critical to our operations and business strategy. Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, ransomware, cyber fraud, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyber-attacks or cyber-intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. Any such breach could compromise our networks and the information stored there

could be accessed, publicly disclosed, encrypted, lost or stolen. Any such access, inappropriate disclosure of confidential or proprietary information or other loss of information, including our data being breached at third-party providers, could result in legal claims or proceedings, liability or financial loss under laws that protect the privacy of personal information, disruption of our operations or the development of our pipeline assets and damage to our reputation, which could adversely affect our business. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, as a result of cyber-attacks we may inadvertently misappropriate assets that we may not be able to fully recover.

We may be subject to future litigation against us, including securities litigation, which could be costly and time-consuming to defend.

The market price of our securities may be volatile, and in the past, companies that have experienced volatility in the market price of their securities have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business. Any adverse determination in litigation could also subject us to significant liabilities.

We may also become subject, from time to time, to legal proceedings and claims that arise in the ordinary course of business such as claims brought by our clients in connection with commercial disputes, or employment claims made by our current or former associates. Litigation might result in substantial costs and may divert management's attention and resources, which might seriously harm our business, overall financial condition, and operating results. Insurance might not cover such claims, might not provide sufficient payments to cover all the costs to resolve one or more such claims, and might not continue to be available on terms acceptable to us. A claim brought against us that is uninsured or underinsured could result in unanticipated costs, thereby reducing our operating results and leading analysts or potential investors to reduce their expectations of our performance, which could reduce the trading price of our stock.

Risks Related to Employee Matters and Managing Our Growth

If we fail to attract and keep management and other key personnel, as well as our board members, we may be unable to develop our product candidates or otherwise implement our business plan.

Our success will depend on the retention of our directors and members of our management and leadership team including Dr. Garry A. Neil, President and Chief Executive Officer, Christopher Sullivan, Chief Financial Officer, Lisa Hegg Ph.D., Senior Vice President of Program Management and Corporate Infrastructure, Colleen Matkowski, Senior Vice President of Global Regulatory Affairs and Quality Assurance, Dino Miano, Senior Vice President, CMC, and Stephen Smolinski, Chief Commercial Officer, and on our ability to continue to attract and retain highly skilled and qualified personnel. From time to time, there may be changes to our executive management team resulting from the hiring or departure of other executives, which could disrupt our business. For example: in February 2022, our then-current Chief Scientific Officer, Garry A. Neil, replaced Michael Cola as our Chief Executive Officer. Additionally, in February 2022, our then-current Chief Accounting Officer, Christopher Sullivan, replaced Schond Greenway as our Chief Financial Officer. The loss of one or more of our executive officers or key associates could have a serious adverse effect on our business.

To continue to executive our business strategy, we must be able to attract and retain highly skilled personnel. We might not be able to attract or retain qualified management and other key personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. Our industry has experienced a high rate of turnover of management personnel in recent years. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts. Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we will have. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are not able to attract and retain the necessary personnel to accomplish our business objectives, we may experience constraints that will impede significantly our ability to implement our business strategy and achieve our business objectives. There can be no assurance that we will retain the services of any of our directors, officers or employees, or attract or retain additional senior managers or skilled employees. Furthermore, we do not intend to carry key man insurance with respect to any of such individuals.

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

As we seek to advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, administrative, 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. 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 additional management, administrative and sales and marketing personnel. The hiring, training and integration of new employees may be more difficult, costly and/or time-consuming for us because we have fewer resources than a larger organization. We might not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing our company.

Our Chief Executive Officer has interests in the development of AVTX-006 pursuant to a royalty agreement that may conflict with interests of stockholders.

Entities affiliated with Dr. Garry Neil, our Chief Executive Officer, are parties to a Royalty Agreement with us relating to AVTX-006. The Royalty Agreement was entered into in July 2019 and we assumed the agreement in the Aevi Merger. The Investors will be entitled to an aggregate amount equal to a low-single digit percentage of the aggregate net sales of AVTX-006 products. At any time beginning three years after the date of the first public launch of AVTX-006 product, we may exercise, at our sole discretion, a buyout option that terminates any further obligations under the Royalty Agreement in exchange for a payment to the Investors of an aggregate of 75% of the net present value of the royalty payments. As a result of this arrangement, the interests of Dr. Neil with respect to our development programs may conflict with the interests of our stockholders. Dr. Neil could make substantial profits as a result of opportunities related to AVTX-006, which may result in him having more interest in advancing programs related to AVTX-006 as opposed to our other pipeline programs. In addition, there would be a conflict of interest if the Company determines to exercise its buyout rights under the Royalty Agreement, the exercise of which would be subject to certain approvals including by our Audit Committee and a majority of our independent directors.

If our employees, independent contractors, principal investigators, CROs, manufacturers, consultants or vendors commit fraud or other misconduct, including noncompliance with regulatory standards and requirements and insider trading, our business may experience serious adverse consequences.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, manufacturers, consultants and vendors may engage in fraudulent 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, (2) manufacturing standards, (3) federal and state healthcare fraud and abuse laws and regulations or (4) laws that require the true, complete and accurate reporting of financial information or data. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. The improper use of information obtained in the course of clinical trials could also result in significant legal sanctions and serious harm to our reputation. In addition, federal procurement laws and regulations impose substantial penalties for misconduct in connection with government contracts and require contractors to maintain a code of business conduct and ethics. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity might 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 regulatory enforcement action, the imposition of significant criminal and civil fines, penalties, or other sanctions, including imprisonment, exclusion from participation in federal healthcare programs, and deferred prosecution and corporate integrity agreements.

In addition, during the course of our operations, our directors, executives and employees may have access to material, nonpublic information regarding our business, our results of operations or potential transactions we are considering. We have adopted an Insider Trading and Window Period Policy, but despite the adoption of such policy, we might not be able to prevent a director, an executive or an employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. If a director, executive or employee was to be investigated, or an action was to be brought against a director, executive or employee for insider trading, it could have a negative impact on our reputation and our stock price. Such a claim, with or without merit, could also result in substantial expenditures of time and money, and divert attention of our management team from other tasks important to the success of our business.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Some of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. We may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. In addition, we may be subject to claims that former employees, collaborators, or other third parties have an ownership interest in our patents or other intellectual property. While it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement to each party who in fact develops intellectual property that we regard as our own. We could be subject to ownership disputes 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 claims.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license might not be available on commercially reasonable terms or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

Risks Related to our Stock

If we are not able to comply with the applicable continued listing requirements or standards of The Nasdaq Stock Market, Nasdaq could delist our common stock.

Our common stock is currently listed on The Nasdaq Stock Market. In order to maintain that listing, we must satisfy minimum financial and other continued listing requirements and standards, including those regarding director independence and independent committee requirements, minimum stockholders' equity, a minimum closing bid price of $1.00 per share, and certain corporate governance requirements. There can be no assurances that we will be able to comply with the applicable listing standards.

In the event that our common stock is delisted from The Nasdaq Stock Market and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further. Also, it may be difficult for us to raise additional capital if we are not listed on a major exchange.

Such a de-listing would also likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a de-listing, we may take actions to restore our compliance with The Nasdaq Stock Market's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below The Nasdaq Stock Market minimum bid price requirement or prevent future non-compliance with The Nasdaq Stock Market's listing requirements.

If the trading price of our common stock fails to comply with the minimum price requirements of The Nasdaq Stock Market, our common stock may be subject to delisting.

Beginning on February 2, 2022, the closing bid price of our common stock has been less than $1.00 per share. If the closing bid price of our common stock remains below the minimum bid price of $1.00 for 30 consecutive trading days, we might receive a letter from the staff of The Nasdaq Stock Market stating that our common stock will be delisted unless we are able to regain compliance with the Nasdaq Listing Rule requiring that we maintain a closing bid price for our common stock of at least $1.00 per share. We cannot guarantee that our stock price will trade above $1.00 per share or otherwise meet the Nasdaq listing requirements and therefore our common stock might in the future be subject to delisting. If our common stock is delisted, this would, among other things, substantially impair our ability to raise additional funds and could result in a loss of institutional investor interest and fewer development opportunities for us.

The market price of our stock is volatile, and you could lose all or part of your investment.

The market price of our shares of our common stock has been highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. From our initial public offering in October 2015 through December 31, 2021, the per share trading price of our common stock has been as high as $7.22 and as low as $0.44. As a result of this volatility, you might not be able to sell your shares of our common stock at a favorable price. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, these factors that could negatively affect or result in fluctuations in the market price of shares of our common stock include:

- our ability to generate significant product revenues, cash flows and a profit;
- the development status of our product candidates, and when any of our product candidates receive marketing approval;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- our failure to commercialize our product candidates, if approved;
- the success of competitive products or technologies;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by our or our competitors of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- results of preclinical studies and clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;

- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- the performance of third parties on whom we rely to manufacture our products and product candidates, supply API and conduct our clinical trials, including their ability to comply with regulatory requirements;
- variations in our financial results or those of companies that are perceived to be similar to us;
- variations in the level of expenses related to our product candidates or preclinical and clinical development programs, including relating to the timing of invoices from, and other billing practices of, our CROs and clinical trial sites;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- warrant or share price and volume fluctuations attributable to inconsistent trading volume levels of our warrants or shares;
- announcement or expectation of additional financing efforts;
- sales of our warrants or shares of our common stock by us, our insiders or our other security holders;
- changes in the structure of healthcare payment systems;
- changes in operating performance and stock market valuations of other pharmaceutical companies;
- market conditions in the pharmaceutical and biotechnology sectors;
- our execution of collaborative, co-promotion, licensing or other arrangements, and the timing of payments we may make or receive under these arrangements;
- additional state and federal healthcare reform measures that could put downward pricing pressure on our products;
- the public's response to press releases or other public announcements by us or third parties, including our filings with the U.S. Securities and Exchange Commission ("SEC") and announcements relating to litigation or other disputes, strategic transactions or intellectual property impacting us or our business;
- announcement related to litigation;
- fluctuations in quarterly operating results, as well as differences between our actual financial and operating results and those expected by investors;
- the financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- changes in financial estimates by any securities analysts who follow our warrants or shares of common stock, our failure to meet these estimates or failure of those analysts to initiate or maintain coverage of our warrants or shares of common stock;
- ratings downgrades by any securities analysts who follow our warrants or shares of common stock;
- the development and sustainability of an active trading market for our shares of common stock;
- future sales of our shares of common stock by our officers, directors and significant stockholders;
- other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events;
- changes in accounting principles; and
- general economic, industry and market conditions.

In addition, the stock market in general, and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of shares of common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this "Risk Factors" section, could have a material adverse impact on the market price of our shares of common stock. When the market price of a stock is volatile, security holders may institute class action litigation against the company that issued the stock. If we become involved in this type of litigation, regardless of the outcome, we could incur substantial legal costs and our management's attention could be diverted from the operation of our business, which could have a material adverse effect on our business, financial condition, results of operations and cash flows.

Future sales and issuances of shares of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to our existing stockholders.

We are authorized to grant equity awards, including stock grants and stock options, to our employees, directors and consultants. As of December 31, 2021, there were 1,570,867 shares available for future issuance under the Third Amended and Restated 2016 Equity Incentive Plan (the "2016 Amended Plan"). During the term of the 2016 Amended Plan, the share reserve will automatically increase on the first trading day in January of each calendar year, by an amount equal to 4% of the total number of outstanding shares of our common stock on the last trading day in December of the prior calendar year. On January 1, 2022, on the terms of the 2016 Amended Plan, an additional 4,511,768 shares were made available for issuance. In addition, as of December 31, 2021, there were 1,735,611 shares available for future issuance under the 2016 Employee Stock Purchase Plan (the "ESPP"). On January 1 of each calendar year, the aggregate number of shares that may be issued under the ESPP will automatically increase by a number equal to the lesser of (i) 1% of the total number of shares of our common stock outstanding on December 31 of the preceding calendar year, and (ii) 500,000 shares of our common stock, or (iii) a number of shares of our common stock as determined by our board of directors or compensation committee. On January 1, 2022, the number of shares available for issuance under the ESPP increased by 500,000 shares available for issuance. Future issuances, as well as the possibility of future issuances, under the 2016 Amended Plan or the ESPP or other equity incentive plans could cause the market price of our common stock to decrease.

Armistice has significant influence over us, and its interests may be different from or conflict with those of our other stockholders.

As of February 22, 2022, Armistice beneficially owns approximately 44% of our outstanding common stock. On December 14, 2021, Steven Boyd, Armistice's Chief Investment Officer, was appointed to Chairman of our board of directors. Armistice also controls two seats on our board of directors, currently occupied by Mr. Boyd and Keith Maher, a managing director at Armistice. As a consequence, Armistice continues to be able to exert a significant degree of influence over our management, affairs, and matters requiring stockholder approval, including the election of directors, a merger, consolidation or sale of all or substantially all of our assets, and any other significant transaction. The interests of Armistice might not always coincide with our interests or the interests of our other stockholders. For instance, this concentration of ownership may have the effect of delaying or preventing a change in control of us otherwise favored by our other stockholders and could depress our stock price.

Armistice makes investments in companies and may, from time to time, acquire and hold interests in businesses that compete directly or indirectly with us. Armistice may also pursue, for its own account, acquisition opportunities that may be complementary to our business, and as a result, those acquisition opportunities might not be available to us. The interests of the Armistice may supersede ours, causing Armistice or their affiliates to compete against us or to pursue opportunities instead of us, for which we have no recourse. Such actions on the part of Armistice and inaction on our part could have a material adverse effect on our business, financial condition, results of operations and cash flows.

Armistice controls two seats on our board of directors. Since Armistice could invest in entities that directly or indirectly compete with us, when conflicts arise between the interests of Armistice and the interests of our stockholders, the directors appointed by Armistice might not be disinterested.

A significant percentage of the outstanding shares of our common stock are held by a single stockholder, which could impact your liquidity, and future sales of shares of our common stock by this stockholder may lower the trading price of shares of our common stock.

As of February 22, 2022, Armistice beneficially owns approximately 44% of our outstanding common stock. Continuation of this concentrated ownership would result in a limited amount of shares being available to be traded in the market, resulting in reduced liquidity. Certain of the shares owned by Armistice have been registered for resale under the Securities Act. Sales of substantial amounts of shares of our common stock by Armistice in the public market, or the perception that such sales will occur, for any reason, could adversely affect the market price of shares of our common stock and make it difficult for it to raise funds through securities offerings in the future.

We have never paid cash dividends on our capital stock, and we do not anticipate paying any cash dividends in the foreseeable future.

The continued operation and expansion of our business will require substantial funding. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. Accordingly, we do not anticipate that we will pay any cash dividends on shares of our common stock for the foreseeable future. Consequently, currently stockholders must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any future gains on their investment. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend upon results of operations, financial condition, contractual restrictions, restrictions imposed by applicable law and other factors our board of directors deems relevant.

We are no longer an "emerging growth company" but qualify as a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

As of December 31, 2020, we lost our status as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. Notwithstanding, we qualify as a "smaller reporting company," which allows us to take advantage of many of the same exemptions from disclosure requirements applicable to us as a former emerging growth company, including not being required to comply with the auditor attestation requirements of Section 404(b) of the Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act") and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict whether investors will find our common stock less attractive because of our reliance on any of 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 incur increased costs and obligations as a result of being a public company.

As a public company, we are required to comply with certain additional corporate governance and financial reporting practices and policies. As a result, due to compliance requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, the listing requirements of the Nasdaq, and other applicable securities rules and regulations, we have and will continue to incur significant legal, accounting, and other expenses. The Exchange Act requires, among other things, that we file annual, quarterly, and current reports with respect to our business and operating results with the SEC. We are also required to ensure that we have the ability to prepare financial statements and other disclosures that are fully compliant with all SEC reporting requirements on a timely basis. Compliance with these rules and regulations has increased and may continue to increase our legal and financial compliance costs, make some activities more difficult, time-consuming, or costly, and increase demand on our systems and resources.

Our amended and restated certificate of incorporation provides that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This choice of forum provision does not preclude or contract the scope of exclusive federal or concurrent jurisdiction for any actions brought under the Securities Act or the Exchange Act. Accordingly, our exclusive forum provision will not relieve us of our duties to comply with the federal securities laws and the rules and regulations thereunder, and our stockholders will not be deemed to have waived our compliance with these laws, rules and regulations.

Any person or entity purchasing or otherwise acquiring any interest in any of our securities will be deemed to have notice of and consented to these provisions. These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum of its choosing for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees.

If a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations, and financial condition. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

Provisions in our amended and restated certificate of incorporation and second amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which we may establish and shares of which we may issue without stockholder approval;

- prohibiting cumulative voting in the election of directors, which would otherwise allow for less than a majority of stockholders to elect director candidates;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

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, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the DGCL which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under the DGCL, a corporation might not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors approved the transaction. Any provision of our amended and restated certificate of incorporation or second amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change of control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our securities.

General Risk Factors

In connection with the reporting of our financial condition and results of operations, we are required to make estimates and judgments which involve uncertainties, and any significant differences between our estimates and actual results could have an adverse impact on our financial position, results of operations and cash flows.

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, expenses and revenues and related disclosure of contingent assets and liabilities. For example, we estimate returns, wholesaler fees, prompt payment discounts, chargebacks and government rebates. We also estimate clinical trial costs incurred using subject data and information from our CROs. If we underestimate or overestimate these expenses, adjustments to expenses may be necessary in future periods. Any significant differences between our actual results and our estimates and assumptions could negatively impact our financial position, results of operations and cash flows.

We may be subject to numerous and varying privacy and security laws, and our failure to comply could result in penalties and reputational damage.

We maintain a large quantity of sensitive information, including confidential business information and information associated with clinical trials. Because of the sensitivity of this information, our privacy and security measures related to such information are very important. Although we have privacy and security measures in place designed to protect sensitive data and our systems, techniques used to obtain unauthorized access or to sabotage systems and data change frequently and often are not recognized until launched against a target. It is also possible that, due to the surreptitious nature of certain data breaches and other incidents, they may remain undetected for an extended period, which may exacerbate harm to the company. We cannot ensure that our privacy and security measures will not be breached or otherwise fail to protect sensitive information or prevent disruption of our operations, including as a result of inadvertent disclosures through technological or human error (including employee or service provider error), malfeasance, hacking, ransomware, social engineering (including phishing schemes), computer viruses, malware, or otherwise. Unauthorized individuals may acquire or obtain unauthorized access to sensitive information. Data breaches, failures of our privacy or security measures, inadvertent disclosures, disruptions of our services, and other incidents could result in serious harm to our reputation, our business might suffer, and we could incur serious liability and other expenses related to litigation (such as damages associated with breach-of-contract claims), penalties for violation of applicable laws or regulations, costly litigation or government investigations, and significant costs for remediation and remediation efforts to prevent future occurrences. The harm associated with these negative results is likely to be exacerbated if the affected information is personally identifiable.

Like others in our industry, we experience cyber-attacks and other attempts to disrupt or gain unauthorized access to our systems on a regular basis. When we become aware of privacy or security incidents, we work diligently to address them, including by working to terminate unauthorized or inappropriate access and implementing additional measures, training, and providing guidance to end users in order to avoid the reoccurrence and future incidents. Although to date, privacy and security incidents have not been material, they could expose us to significant expense, legal liability, and harm to our reputation, which might result in an adverse impact our operating results.

We are subject to certain laws and regulations governing the privacy and security of personal information, including regulations pertaining to health information. The legislative and regulatory landscape for privacy and data security continues to evolve, and there has been an increasing focus on privacy and data security issues that may affect our business. In the United States, there are numerous federal and state privacy and data security laws and regulations that govern the collection, use, disclosure, and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. Each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. If we fail to comply with applicable laws and regulations, we could be subject to lawsuits, penalties, or sanctions. The HHS Office for Civil Rights, which enforces HIPAA, remains active in its enforcement of the law. Additionally, state attorneys general may bring civil actions seeking either injunctions or damages in response to violations of HIPAA that threaten the privacy of state residents. Privacy and data security has become an area of emphasis for some state legislatures. For example, the California Privacy Rights Act, the Colorado Privacy Act, and the Virginia Consumer Data Protection Act were all enacted recently and will become operative in 2023. (Some provisions are already operative.) State legislatures may pass additional privacy and data security laws with inconsistent requirements. In addition to the risk associated with enforcement, compliance with and implementation of these evolving laws, rules, and regulations regarding the privacy, security and protection of personal information could result in higher compliance and technology costs for us and present challenges for our business model.

There are numerous federal and state laws that generally require notice to affected individuals, regulators, and sometimes the media or credit reporting agencies in the event of a data breach impacting personal information. For example, at the federal level, HIPAA Breach Notification Rule mandates notification of breaches affecting protected health information to affected individuals and regulators under conditions set forth in the Rule. Covered entities must report breaches of unsecured protected health information to affected individuals without unreasonable delay, but not to exceed 60 days of discovery of the breach by a covered entity or its agents. Notification must also be made to HHS and, in certain circumstances involving large breaches, to the media. Business Associates must report breaches of unsecured protected health information to covered entities. All states, the District of Columbia, Guam, Puerto Rico, and the Virgin Islands have enacted data breach notification laws. These laws may impose notification obligations in addition to, or inconsistent with, the HIPAA Breach Notification Rule when a data breach implicates protected health information. In that event that we fail to detect or timely report a data breach it may be subject to significant penalties under federal and state law. In the event that we report a data breach as required by federal or state law, federal or state regulators may initiate an investigation into, and/or litigation related to, our privacy or data security practices. Private plaintiffs may also initiate costly class action litigation following a data breach.

Numerous other countries have, or are developing, laws governing the collection, use, and transmission of personal information. These laws often impose significant compliance obligations. For example, the General Data Protection Regulation ("GDPR") has imposed stringent obligations and restrictions on the ability to collect, analyze, and transfer personal information, including health data from clinical trials and substantial fines for breaches of the data protection rules in the European Economic Area ("EEA"). To the extent that our activities are or become subject to the GDPR, we may need to devote significant effort and resources to complying with those legal regimes. Any failure to comply with the rules arising from the GDPR could lead to government enforcement actions and significant penalties against us and adversely impact our operating results. If our operations are found to violate GDPR requirements, we may incur substantial fines, have to change our business practices, and face reputational harm, any of which could have an adverse effect on our business. In particular, serious breaches of the GDPR can result in administrative fines of up to 4% of annual worldwide revenues. Fines of up to 2% of annual worldwide revenues can be levied for other specified violations. The validity of data transfer mechanisms remains subject to legal, regulatory, and political developments in both Europe and the United States, such as recent recommendations from the European Data Protection Board, the invalidation of the EU-U.S. Privacy Shield, and potential invalidation of other data transfer mechanisms, which could have a significant adverse impact on our ability to process and transfer personal data outside of the EEA. These developments create some uncertainty, and compliance obligations could cause us to incur costs or harm the operations of our products and services in ways that harm our business.

Our disclosure controls and procedures might not prevent or detect all errors or acts of fraud.

We are subject to the periodic reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and The Nasdaq Stock Market rules and regulations. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. We cannot assure, in the future, a material weakness or significant deficiency will not exist or otherwise be discovered. If that were to happen, it could harm our operating results and cause stockholders to lose confidence in our reported financial information. Any such loss of confidence would have a negative effect on the trading price of our securities.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Low trading volume of our common stock on the Nasdaq Capital Market may increase price volatility.

Our common stock may be subject to price volatility, low trading volume and large spreads in bid and ask prices quoted by market makers. Due to the low volume of shares traded on any trading day, persons buying or selling in relatively small quantities may easily influence prices of our common stock. This low trading volume could also cause the price of our stock to fluctuate greatly, with large percentage changes in price occurring in any trading day session. Holders of our common stock may also not be able to readily liquidate their investment or may be forced to sell at depressed prices due to low trading volume. If large spreads between the bid and ask prices of our common stock exist at the time of a purchase, the stock would have to appreciate substantially on a relative percentage basis for an investor to recoup their investment. No assurance can be given that a higher volume active market in our common stock will develop or be sustained. If a higher volume active market does not develop, holders of our common stock may be unable to readily sell the shares they hold or may not be able to sell their shares at all.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. As additional shares of our common stock become available for resale in the public market pursuant to this offering, and otherwise, the supply of our common stock will increase, which could decrease its price. In addition, some or all of the shares of common stock may be offered from time to time in the open market pursuant to Rule 144, and these sales may have a depressive effect on the market for our shares of common stock. Therefore, we cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

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

The trading market for our securities will depend in part on the research and reports that securities or industry analysts publish about us or our business. We currently have limited, and might not sustain, research coverage by securities and industry analysts. If we do not sustain coverage of ourselves, the trading price for securities would be negatively impacted. If the securities and industry analysts are unable to predict accurately the cost of advancing our pipeline, that could result in our reported costs being different than expectations, which could negatively affect our stock price. If we do obtain securities or industry analyst coverage and if one or more of the analysts who covers us downgrades our securities or publishes inaccurate or unfavorable research about our business, our securities prices would likely decline. If one or more of these analysts ceases coverage of us or fails to publish reports on us regularly, demand for our securities could decrease, which could cause our securities prices and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our headquarters are located in Rockville, Maryland, where we occupy approximately 5,000 square feet of administrative office space. The lease expires January 31, 2030.

The Company also occupies approximately 11,000 square feet of administrative office space in Chesterbrook, Pennsylvania. The lease expires on February 28, 2027.

We believe that our existing facilities are adequate to meet our current needs, and that suitable spaces will be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock is listed and publicly traded on The Nasdaq Capital Market under the symbol "AVTX."

Holders

As of February 28, 2022, there were approximately 100 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

Dividends

We have never declared or paid cash dividends on our capital stock. We intend to retain all of our available funds and future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Recent Sales of Unregistered Securities

Except for sales of unregistered securities that have been previously reported by the Company in either its quarterly reports on Form 10-Q or current reports on Form 8-K, there were no sales of unregistered securities of the Company during the period covered by this report.

Equity Compensation Plans

See Item 12 of this report for disclosure regarding securities authorized for issuance under equity compensation plans required by Item 201(d) of Regulation S-K.

Item 6. Reserved.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section in this Annual Report on Form 10-K for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

Avalo Therapeutics, Inc. (the "Company," "Avalo" or "we") is a leading clinical-stage precision medicine company that discovers, develops, and commercializes targeted therapeutics for patients with significant unmet clinical need in immunology and rare genetic diseases. We have built a diverse portfolio of innovative therapies to deliver meaningful medical impact for patients in urgent need. Our clinical candidates commonly have a proven mechanistic rationale, biomarkers and/or an established proof-of-concept to expedite development and increase the probability of success.

The Company's focus in 2021 was on progressing the pipeline and executing financing activities to fund pipeline development. These will also be the primary areas of focus in 2022, with a broader focus on both non-dilutive and dilutive funding opportunities and potential business development related opportunities such as the out-license or partnering of assets. Management's primary evaluation of the success of the Company is the ability to progress its pipeline assets forward towards commercialization or opportunistically out-license rights to indications or geographies. This success depends on not only the operational execution of the programs, but also the ability to secure sufficient funding to support the programs. We believe the ability to achieve the anticipated milestones as presented in the section entitled "Business" in Item 1 of this Annual Report on Form 10-K represents our most immediate evaluation points.

In 2021, we believe that we made significant progress in advancing our pipeline as reported during the year highlighted by the data release of the first two cohorts of the AVTX-002 Phase 1b trial in Crohn's Disease, data release of the AVTX-002 Phase 2 proof-of-concept trial in COVID-19 ARDS and subsequent receipt of fast-track designation ("FTD"), receipt of FTD for AVTX-803 and enrollment of the first patient in the AVTX-007 Phase 1b open-label proof-of-concept trial in adult onset Still's Disease. We also believe our licensing activity in the first half of 2021, including in-licenses of immunology and immuno-oncology assets (including the expanded license agreement for AVTX-002 and the license agreement of AVTX-008) and out-licenses of non-core assets, enhances our focus on the development of innovative therapies in areas of high unmet need within the fields of immunology and rare genetic disorders. Additionally, we executed financings in 2021 for total net proceeds of approximately $105 million, which served to strengthen and extend our financial resources to advance our clinical pipeline towards key development milestones.

Recent Updates

In February 2022, Dr. Garry Neil and Chris Sullivan were promoted to Chief Executive Officer and Chief Financial Officer, respectively. In early 2022, management has been focused on developing and beginning to execute an optimal strategy of prioritizing our most promising programs. As a result, we are winding down internal development efforts of AVTX-006 and AVTX-007 in multiple myeloma (previously announced in January 2022) and pausing current development efforts of AVTX-802. We plan to pursue strategic alternatives for AVTX-006. Regarding AVTX-802, current development has been paused due to an impasse related to FDA regulatory requirements of the trial design and feasibility based upon investigator feedback and will re-evaluate development plans in the event of an alignment with the FDA on the trial design. Additionally, we will not proceed with the extension of the Phase 1b, open-label trial in a cohort of ulcerative colitis ("UC") patients with moderate to severe UC who are refractory to biologic therapy given the positive data we previously received in Crohn's disease patients and the similarity of the conditions. Alternatively, we will consider a possible randomized, double-blind, placebo-controlled trial in moderate to severe refractory patients with IBD. Finally, we will conduct a new Phase 2 randomized, double-blind, placebo-controlled trial of AVTX-002 for the treatment of moderate to severe Non-eosinophilic Asthma and expect top-line data in the fourth quarter of 2022.

Impact of COVID-19 Pandemic

As of the filing date of this Annual Report on Form 10-K, we have not experienced significant financial impact directly related to the COVID-19 pandemic, however we have experienced some disruptions to clinical operations and manufacturing of drug supply for use in clinical trials. For example, we have experienced a slower pace of patient enrollment at many of our clinical trial sites than our initial projections. Some of our clinical sites have experienced challenges in conducting trial activities while they focus resources on COVID-19 patients and due to facility restrictions, remote work requirements and other precautions. Additionally, we have experienced manufacturing delays of drug product due to the limited available capacity of certain of our manufacturers due to staffing shortages, production slowdowns because of overall increased manufacturing in the biotechnology industry, as well as increased

manufacturing of COVID-19 vaccines. We have worked (and will continue to work) closely with our third-party contractors, investigators and manufacturers to ensure our ongoing clinical trials proceed safely and efficiently. We will continue to assess the potential impact of COVID-19 pandemic on our business and operations, including our clinical operations and manufacturing activities.

2021 Financial Operations Overview

Research and development expense for the year ended December 31, 2021 significantly increased as compared to the prior year, which was driven by the advancement of our maturing pipeline. Notably, we incurred significant expenses related to the clinical development of AVTX-002, which included increased drug manufacturing to support clinical trials. We also recognized a $10 million upfront license fee related to the expanded indication license agreement for AVTX-002 entered into with KKC during the year. In addition, there were moderate increases to program costs for AVTX-007, AVTX-006 and AVTX-803 as we progressed the therapies toward pivotal trials. There was also a moderate increase to general and administrative expense related to the infrastructure needed to support the Company's expansion of its research and development efforts. Such increases were the main drivers to our net loss of $84.4 million for the year ended December 31, 2021. Additionally, our net cash used in operations increased by $30.4 million for the year ended December 31, 2021, which was also driven by the advancement of our maturing pipeline. We do not expect a similar increase to operating expenses in 2022. Rather, it is likely we will incur similar operating expenses to begin 2022 as we finished 2021. Expenses beyond the start of 2022 are difficult to predict given it will be highly dependent on study outcomes, business development initiatives and access to capital. Furthermore, it is possible the recent and continued portfolio prioritization may result in decreases to research and development expenses and supporting general and administrative and marketing expenses in the intermediate future, while also potentially driving increases to expenses such as severance and wind down costs in the short term.

As of December 31, 2021, Avalo had $54.6 million in cash and cash equivalents, representing a $35.7 million increase as compared to December 31, 2020. The increase was driven by financings executed during the year partially offset by operating expenditures. We plan to use our current cash on hand along with cash inflows from investing and/or financing activities to support the ongoing clinical development of our maturing pipeline and for general corporate purposes to support such pipeline development.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

Product Revenue, net

Net product revenue was $4.8 million for the year ended December 31, 2021, compared to $6.7 million for the year ended December 31, 2020. While gross sales were higher in 2021 as compared to 2020, there was a decrease in net sales driven by a significant increase in sales return allowance due to a full return allowance on sales of short-dated inventory sold in the first quarter of 2021 and due to a $0.5 million accounts receivable write-off of remaining uncollected balances on sales managed by Aytu Bioscience, Inc. ("Aytu").

The Company began managing commercial operations of Millipred® in the third quarter of 2021. Aytu, to which the Company sold its rights, title and interest in assets relating to certain commercialized products in 2019, managed Millipred® commercial operations until August 31, 2021. The transition may have caused disruptions to the sales channel potentially impacting units sold in the fourth quarter, thus contributing to the decrease in net product revenue.

License Revenue

License revenue was $0.6 million for the year ended December 31, 2021, which relates to upfront fees received as a result of the out-license and assignment, respectively, of the Company's rights to its non-core neurology pipeline assets, AVTX-301 and AVTX-406 to Alto Neurosciences, Inc. ("Alto") and ES Therapeutics, LLC ("ES"), respectively. ES is a wholly-owned subsidiary of Armistice, which is a significant stockholder of the Company and whose chief investment officer, Steven Boyd, and managing director, Keith Maher, currently serve on the Board of the Company. The transaction with ES was approved in accordance with Avalo's related party transaction policy. There was no license revenue for the year ended December 31, 2020.

Avalo is eligible to receive additional payments upon achievement of specified development, regulatory and sales-based milestones for both AVTX-301 and AVTX-406 and is also entitled to royalty payments based on net sales of AVTX-301.

Cost of Product Sales

Cost of product sales were $1.5 million for the year ended December 31, 2021, as compared to $0.3 million for the year ended December 31, 2020. The increase was primarily driven by the Company's requirement to pay its supplier fifty percent of the net profit of the Millipred® product following each calendar quarter beginning on July 1, 2021, subject to a $0.5 million quarterly minimum payment. We expect cost of product sales to increase as compared to historic periods prior to the profit share beginning.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Preclinical expenses	$ 6,673	$ 6,487
Clinical expenses	14,055	10,803
CMC expenses	17,000	7,645
License and milestone expenses	10,900	—
Internal expenses:		
Salaries, benefits and related costs	9,114	5,763
Stock-based compensation expense	1,775	1,340
Other	318	155
	$ 59,835	$ 32,193

Research and development expenses increased $27.6 million for the year ended December 31, 2021, compared to the year ended December 31, 2020. The overall increase was driven by an increase in research and development activities in 2021 as the Company continues to develop its maturing pipeline assets.

The increase was driven by a $10 million upfront license fee, related to the expanded indication license agreement for AVTX-002 entered into with KKC in March 2021. Additionally, CMC expenses increased $9.4 million due to increased manufacturing to support development of the progressing pipeline and in anticipation of drug supply to support clinical trials. Clinical expenses increased $3.3 million due to costs incurred to advance the pipeline as we approach multiple clinical data read outs across our pipeline. Finally, salaries, benefits and related costs increased by $3.4 million mainly due to an increase in headcount to grow our research and development activities to support our maturing pipeline.

We do not expect a similar increase to research and development expenses in 2022. Rather, it is likely we will incur similar expenses to begin 2022 as we finished 2021. Research and development expenses beyond the start of 2022 are difficult to predict given it will be highly dependent on study outcomes, business development initiatives and access to capital.

Acquired In-Process Research and Development Expenses

In the first quarter of 2020, the Company consummated its merger with Aevi, resulting in us acquiring $25.5 million of in-process research and development ("IPR&D"). The fair value of the IPR&D was immediately recognized as acquired in-process research and development expense given such asset has no other alternate use due to the stage of development. There was no acquired in-process research and development expense for the year ended December 31, 2021.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Salaries, benefits and related costs	$ 4,561	$ 4,704
Legal, consulting and other professional expenses	10,029	6,606
Stock-based compensation expense	5,983	5,131
Other	1,259	977
	$ 21,832	$ 17,418

General and administrative expenses increased $4.4 million for the year ended December 31, 2021 compared to the same period in 2020. The increase was largely driven by a $3.4 million increase in legal, consulting and other professional expenses. The largest driver was higher legal expenses in the current period, including costs to execute the KKC expanded indication license agreement and the other licensing agreements executed in the year. Additionally, there were increases to information technology services, consulting and director and officer insurance. Such increases were partially offset by a legal settlement in the prior period that did not repeat in the current period. Stock-based compensation expense increased $0.9 million for the year ended December 31, 2021, which was attributable to new grants, including the annual stock option grant, and modifications to certain existing awards.

Sales and Marketing Expenses

The following table summarizes our sales and marketing expenses for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Salaries, benefits and related costs	$ 641	$ 749
Stock-based compensation expense	414	315
Advertising and marketing expense	1,657	1,240
Other	114	37
	$ 2,826	$ 2,341

Sales and marketing expenses primarily consist of expenses related to initiatives to support the go-to-market strategy of our pipeline assets. Sales and marketing expense increased $0.5 million for the year ended December 31, 2021 compared to the same period in 2020, which was largely driven by market research projects for multiple programs and indications and marketing expense related to the corporate name change to Avalo Therapeutics, Inc.

Amortization Expense

The following table summarizes amortization expense for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Amortization of intangible assets	$ 1,548	$ 1,741

For the year ended December 31, 2021, amortization expense consisted of the amortization of our intangible assets including product marketing rights acquired as part of a previous acquisition and an assembled workforce acquired as part of a previous merger. The product marketing rights asset was fully amortized in the fourth quarter of 2021, thus driving the decrease for the year ended December 31, 2021 as compared to the prior year.

We expect amortization expense to decrease as compared to historical periods given the product marketing rights asset was fully amortized in the fourth quarter of 2021 and the assembled workforce will be fully amortized in the first quarter of 2022.

Other (Expense) Income, net

The following table summarizes our other (expense) income, net from continuing operations for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Change in fair value of Investment in Aytu (as defined below)	$ —	$ 5,208
Other (expense) income, net	(20)	409
Interest (expense) income, net	(2,391)	49
	$ (2,411)	$ 5,666

Other expense, net was comprised of interest expense of $2.4 million for the year ended December 31, 2021. The interest expense recognized related to the venture debt financing agreement entered into in June 2021. We expect interest expense to increase in 2022 as a result of recognizing a full year of interest.

For the year ended December 31, 2020, other income, net was mainly comprised of a $5.2 million gain on change in the fair value of an investment. As consideration of the Company's sale of its rights, title and interest in assets relating to certain commercialized products to Aytu in 2019, the Company received 9.8 million shares of Aytu preferred stock (the "Investment in Aytu"), which was remeasured at fair value each reporting period. In 2020, the Company sold the underlying Aytu common stock for net proceeds of $12.8 million, which represented a gain of $5.2 million from its fair value as of the period prior to the sale.

Income Tax Benefit

The Company recognized an income tax benefit of $0.2 million for the year ended December 31, 2021 and $2.8 million for the year ended December 31, 2020. The income tax benefit recognized in the current year was the result of the receipt of the Company's federal refund in 2021 along with an additional $0.2 million related to additional interest received. The tax benefit recognized for the year ended December 31, 2020 was a result of a tax law change and the ability of the Company to carry back certain losses related to the CARES Act and related state provisions. The annual effective tax rate was 0.22% and 4.21% for the years ended December 31, 2021 and 2020, respectively.

Liquidity and Capital Resources, including Capital Expenditure and Cash Requirements

As of December 31, 2021, Avalo had $54.6 million in cash and cash equivalents. In 2021, the Company closed three equity offerings for net proceeds of approximately $72.0 million (see Note 12 to the consolidated financial statements for more information). In June 2021, the Company entered into a $35 million venture debt financing agreement (the "Loan Agreement") with Horizon Technology Finance Corporation ("Horizon") and Powerscourt Investments XXV, LP ("Powerscourt", together with Horizon, the "Lenders"). As of December 31, 2021, the Company had received the full $35 million. The Loan Agreement contains certain covenants and certain other specified events that could result in an event of default, which if not cured or waived, could result in the immediate acceleration of all or a substantial portion of the notes. As of the filing date of this Annual Report on Form 10-K, the Company was not aware of any breach of covenants, occurrence of material adverse change, nor had it received any notice of event of default from the Lenders (see Note 11 to the consolidated financial statements for more information).

In order to meet its cash flow needs, the Company applies a disciplined decision-making methodology as it evaluates the optimal allocation of the Company's resources between investing in the Company's existing pipeline assets and acquisitions or in-licensing of new assets. For the year ended December 31, 2021, Avalo generated a net loss of $84.4 million and negative cash flows from operations of $70.9 million. As of December 31, 2021, Avalo had an accumulated deficit of $262.2 million.

The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern; however, losses are expected to continue as the Company continues to invest in its core research and development pipeline assets. The Company will require additional financing to fund its operations and to continue to execute its business strategy at least one year after the date the financial statements included herein were issued. These conditions raise substantial doubt about the Company's ability to continue as a going concern.

To mitigate these conditions and to meet the Company's capital requirements, management plans to use its current cash on hand along with some combination of the following: (i) dilutive and/or non-dilutive financings, (ii) federal and/or private grants, (iii) other out-licensing or strategic alliances/collaborations of its current pipeline assets, and (iv) out-licensing or sale of its non-core assets. If the Company raises additional funds through collaborations, strategic alliances or licensing arrangements with third parties, the Company might have to relinquish valuable rights to its technologies, future revenue streams, research programs or product candidates. Subject to limited exceptions, our venture debt financing agreement prohibits us from incurring certain additional indebtedness, making certain asset dispositions, and entering into certain mergers, acquisitions or other business combination transactions without prior consent of the Lenders. If the Company requires but is unable to obtain additional funding, the Company may be forced to make reductions in spending, delay, suspend, reduce or eliminate some or all of its planned research and development programs, or liquidate assets where possible. Due to the uncertainty regarding future financing and other potential options to raise additional funds, management has concluded that substantial doubt exists with respect to the Company's ability to continue as a going concern within one year after the date that the financial statements in this Annual Report on Form 10-K were issued.

Over the long term, the Company's ultimate ability to achieve and maintain profitability will depend on, among other things, the development, regulatory approval, and commercialization of its pipeline assets, and the potential receipt and sale of any priority review vouchers it receives.

Uses of Liquidity

The Company uses cash to primarily fund the ongoing development of our research and development pipeline assets and costs associated with its organizational infrastructure.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash (used in) provided by:		
Operating activities	$ (70,892)	$ (40,539)
Investing activities	(113)	11,132
Financing activities	106,762	44,784
Net increase in cash and cash equivalents	$ 35,757	$ 15,377

Net cash used in operating activities

Net cash used in operating activities was $70.9 million for the year ended December 31, 2021, and consisted primarily of a net loss of $84.4 million, which was driven by increased research and development activities as the Company continued to fund its maturing pipeline of development assets, and non-cash adjustments to reconcile net loss to net cash used in operating activities including stock-based compensation of $8.2 million. Additionally, changes in net liabilities increased by $2.8 million. The increase was mainly driven by a $3.2 million increase in accrued expenses and $1.1 million decrease in accounts receivable, partially offset by an increase of $1.5 million in other receivables.

We expect to continue to use significant amounts of cash related to operating activities as we advance our pipeline.

Net cash used in operating activities was $40.5 million for the year ended December 31, 2020, and consisted primarily of a net loss of $63.5 million and non-cash adjustments to reconcile net loss to net cash used in operating activities including the $5.2 million realized gain related to the change in fair value of the Investment in Aytu. This decrease was offset mainly by a non-cash acquired IPR&D expense of $25.5 million and non-cash stock-based compensation of $6.8 million.

Net cash (used in) provided by investing activities

Net cash used in investing activities was $0.1 million for the year ended December 31, 2021 and consisted primarily of the purchase of property and equipment.

Net cash provided by investing activities was $11.1 million for the year ended December 31, 2020, and consisted primarily of net proceeds of $12.8 million from the sale of Aytu common stock underlying the Company's previous Investment in Aytu, slightly offset by transaction costs incurred as part of the Aevi Merger.

Net cash provided by financing activities

Net cash provided by financing activities was $106.8 million for the year ended December 31, 2021, consisting primarily of net proceeds of $104.9 million from equity and debt financings. Specifically, the Company received net proceeds of $37.7 million from an underwritten public offering closed in January 2021, net proceeds of $32.9 million from the Loan Agreement entered into in the second quarter of 2021 and net proceeds of $29.0 million from an underwritten public offering that closed in September 2021.

We expect to continue to engage in financing activities to support clinical development.

Net cash provided by financing activities was $44.8 million for the year ended December 31, 2020 and consisted primarily of net proceeds of $35.4 million from an underwritten public offering of common stock. The Company also received net proceeds of $5.1 million from a registered direct offering with certain institutional investors, which included Armistice, that closed in February 2020, and net proceeds of $3.9 million from a private placement of equity securities with Armistice in March 2020.

Critical Accounting Estimates and Assumptions

In preparing the financial statements, the Company makes estimates and assumptions that have an impact on assets, liabilities, revenue and expenses reported. These estimates can also affect supplemental information disclosed by us, including information about contingencies, risk and financial condition. The Company believes, given current facts and circumstances, our estimates and assumptions are reasonable, adhere to GAAP and are consistently applied. Inherent in the nature of an estimate or assumption is the fact that actual results may differ from estimates, and estimates may vary as new facts and circumstances arise.

While our significant accounting policies are more fully described in Note 2 to the audited consolidated financial statements appearing at the end of this Annual Report on Form 10-K, we believe the following accounting policy is critical to the understanding of our financial condition and results.

Stock-Based Compensation

The Company applies the provisions of ASC 718, Compensation—Stock Compensation, which requires the measurement and recognition of compensation expense for all stock-based awards made to employees, including employee stock options, in the statements of operations and comprehensive loss.

For stock options issued to employees and members of the board of directors for their services, the Company estimates the grant date fair value of each option using the Black-Scholes option pricing model. The use of the Black-Scholes option pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. Additionally, the stock price on the date of grant is utilized in the Black-Scholes option pricing model. For awards subject to service-based vesting conditions, including those with a graded vesting schedule, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period, which is generally the vesting term. Forfeitures are recorded as they are incurred as opposed to being estimated at the time of grant and revised.

The assumptions we used to determine the fair value of stock options granted to employees and members of the board of directors are as follows:

	Year Ended December 31,					
Service-based options	**2021**			**2020**		
Expected term of options (in years)	0.76	—	6.25	1.75	—	6.25
Expected stock price volatility	73.0%	—	86.5%	69.9%	—	79.0%
Risk-free interest rate	0.07%	—	1.34%	0.19%	—	1.48%
Expected annual dividend yield	0%			0%		

The estimates involved in the valuations include inherent uncertainties and the application of our judgment. As a result, if factors change and we use significantly different assumptions or estimates when valuing our stock options, our stock-based compensation expense could be materially different. We recognize compensation expense for only the portion of awards that are expected to vest.

Debt Financing Agreement and Warrants

In the June 2021, the Company entered into a $35 million venture debt financing agreement, under which the Company borrowed $20 million at closing and borrowed an additional $15 million upon the achievement of certain predetermined milestones. Pursuant to the Loan Agreement, the Company issued warrants to the Lenders to purchase an aggregate of 403,844 shares of the Company's common stock with an exercise price of $2.60 (the "Warrants").

We applied judgement in evaluating the identification of each instrument and feature requiring separate accounting recognition and determination of whether each should be classified as a liability or in stockholders' equity. The issuance of debt and Warrants in one transaction resulted in estimating the fair values of each instrument and feature.

We allocated consideration received to the debt and Warrants (which we concluded met equity classification criteria and therefore recognized as a component of permanent stockholders' equity within additional paid-in-capital) based on the relative fair value allocation method. We valued the Warrants at issuance, which resulted in a discount on the debt, and allocated proceeds proportionately to the debt and to the Warrants.

The debt is recorded on the balance sheet at carrying value, which is the gross balance, less the unamortized debt discount and issuance costs. All fees, costs paid to the Lenders, and all direct costs incurred by the Company are recognized as a debt discount and are amortized to interest expense using the effective interest method of the life of the loan.

Off-Balance Sheet Arrangements

The Company does not have any off-balance sheet arrangements, as defined by applicable SEC rules and regulations.

Recently Adopted Accounting Pronouncements

For a discussion of new accounting standards please see Note 2 to consolidated financial statements contained in this Annual Report on Form 10-K.

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

As a smaller reporting company, we are not required to provide the information required by this Item.

Item 8. Financial Statements and Supplementary Data.

The consolidated financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those consolidated financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

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

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, as of the end of the period covered by this report.

In designing and evaluating our disclosure controls and procedures, management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply its judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Based on their evaluation, our principal executive officer and principal financial officer concluded that as of December 31, 2021, our disclosure controls and procedures are designed to, and are effective to, provide assurance at a reasonable level that the information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosures as of December 31, 2021.

Management's Annual Report on Internal Control Over Financial Reporting

Our management, including our principal executive officer and principal financial officer, is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act). Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Our internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2021, based on the Internal Control-Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework). Based on this evaluation under the 2013 Framework, our principal executive officer and principal financial officer have concluded that our internal control over financial reporting was effective at a reasonable level of assurance as of December 31, 2021.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the most recent fiscal quarter that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Attestation Report of Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exclusion for certain smaller reporting companies.

Item 9B. Other Information.

On February 8, 2022, the Company filed a Form 8-K with the Securities and Exchange Commission disclosing that on February 2, 2022, H. Jeffery Wilkins resigned as Chief Medical Officer, effective upon a date to be agreed upon. Dr. Wilkins' resignation will be effective on March 21, 2022.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspection.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this Item concerning our directors and executive officers is incorporated by reference from the sections captioned "Election of Directors", "Executive Officers" and "Corporate Governance Matters" contained in our definitive proxy statement related to the 2022 Annual Meeting of Stockholders to be filed with the SEC with 120 days after the end of the fiscal year pursuant to General Instruction G(3) of Form 10-K (the "Proxy Statement").

The information required by this Item concerning our Audit Committee is incorporated by reference from the section of the proxy statement captioned "Information Regarding the Board and Corporate Governance – Information Regarding Committees of the Board – Audit Committee".

The Company has adopted the Avalo Therapeutics, Inc. Code of Business Conduct and Ethics that applies to all officers, directors and employees. The Code of Business Conduct and Ethics is available on the Company's website at ir.avalotx.com. If the Company makes any substantive amendments to the Code of Business Conduct and Ethics or grants any waiver from a provision of the Code to any executive officer or director, the Company will promptly disclose the nature of the amendment or waiver on its website.

Item 11. Executive Compensation.

The information required by this Item is incorporated by reference to the information under the sections of the proxy statement captioned "Executive Compensation" and "Director Compensation".

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

The following table contains certain information with respect to our equity compensation plans (including individual compensation arrangements) in effect as of December 31, 2021:

	(A)		(B)		(C)	
Plan category	**Number of Securities to be Issued Upon Exercise of Outstanding Options and Vesting of Restricted Stock Units (#)**		**Weighted-Average Exercise Price of Outstanding Options ($)**		**Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans, excluding securities reflected in column (A) (#)**	
Equity compensation plans approved by stockholders	13,162,228		$3.66	(1)	1,570,867	(2)
Equity compensation plans not approved by stockholders	500,000	(3)	$3.73		—	
Total	13,662,228		$3.66	(1)	1,570,867	

(1) The weighted-average exercise price does not take into account shares issuable upon the vesting of outstanding restricted stock units, which have no exercise price. As of December 31, 2021, there were 11,250 shares of unvested restricted stock units.

(2) Reflects shares of common stock available for future issuance under our Third Amended and Restated 2016 Equity Incentive Plan at December 31, 2021. In March 2018, our board of directors adopted the Amended and Restated 2016 Equity Incentive Plan, which was approved by our stockholders in May 2018.

In June 2019, our board of directors adopted the Second Amended and Restated 2016 Equity Incentive Plan, which was approved by our stockholders in August 2019. In April 2020, our board of directors adopted the Third Amended and Restated Equity Incentive Plan, which was approved by our stockholders in June 2020. During the term of the Third Amended and Restated 2016 Equity Incentive Plan, the share reserve will automatically increase on the first trading day in January of each calendar year, by an amount equal to 4% of the total number of outstanding shares of common stock of the Company on the last trading day in December of the prior calendar year. On January 1, 2022, pursuant to the terms of the Third Amended and Restated Equity Inventive Plan an additional 4,511,768 shares were made available for issuance.

(3) Consists of shares of common stock issuable upon exercise of outstanding stock options granted pursuant to the Nasdaq inducement grant exception as a component of employment compensation for employees. The inducement grant was made as an inducement material to Mr. Greenway, the Company's former Chief Financial Officer, entering into employment with us in accordance with Nasdaq Listing Rule 5635(c)(4). The option was set to vest over four years, with one-quarter of such options vesting on the first anniversary of the grant date and the remaining three-quarters of the options vesting in equal monthly installments over the following 36 months, in each case, subject to continued employment with the Company through the applicable vesting date. Mr. Greenway was separated from the Company on February 14, 2022. Pursuant to his separation agreement, effective on February 14, 2022, the shares subject to this option that would have vested in the twelve months following the separation date immediately vested and are exercisable through February 14, 2023.

The other information required by this Item is incorporated by reference to the information under the section captioned "Security Ownership of Certain Beneficial Owners and Management" contained in the proxy statement.

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

The information required by this Item is incorporated by reference to the information under the sections of the proxy statement captioned "Transactions with Related Persons" and "Information Regarding the Board and Corporate Governance – Independence of the Board".

Item 14. Principal Accounting Fees and Services.

The information required by this Item is incorporated by reference to the information under the section of the proxy statement captioned "Information Regarding the Board and Corporate Governance – Information Regarding Committees of the Board – Audit Committee – Report of the Audit Committee of the Board".

PART IV

Item 15. Exhibits; Financial Statement Schedules.

(a) *Documents filed as part of this report.*

1. The following consolidated financial statements of Avalo Therapeutics, Inc. and Report of Ernst & Young LLP, Independent Registered Public Accounting Firm, are included in this report:

2. List of financial statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the financial statements described above.

3. List of Exhibits required by Item 601 of Regulation S-K. See part (b) below.

(b) *Exhibits.*

The following is a list of exhibits filed as part of this Annual Report on Form 10-K. Where so indicated by footnote, exhibits that were previously filed are incorporated by reference. For exhibits incorporated by reference, the location of the exhibit in the previous filing is indicated.

Exhibit Number	Description of Exhibit
2.1	Asset Purchase Agreement, dated October 10, 2019, between Aytu Bioscience, Inc. and Cerecor Inc. (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed on October 15, 2019).
2.2	First Amendment to Asset Purchase Agreement, dated November 1, 2019, entered into by and between Aytu Bioscience, Inc. and Cerecor Inc. (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K filed on November 4, 2019).
2.3	Agreement and Plan of Merger and Reorganization, dated as of December 5, 2019, by and among Cerecor Inc., Genie Merger Sub, Inc., Second Genie Merger Sub, LLC and Aevi Genomic Medicine, Inc. (incorporated by reference to Exhibit 2.1 to the Current Report on Form 8-K/A filed on December 11, 2019).
3.1	Amended and Restated Certificate of Incorporation of Cerecor Inc. (incorporated by reference to Exhibit 3.1.2 to the Current Report on Form 8-K filed on May 17, 2018).
3.1.1	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Cerecor Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed on August 26, 2021).
3.1.2	Form of Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock of Cerecor Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed on April 28, 2017).

3.1.3	Form of Certificate of Designation of Series B Non-Voting Convertible Preferred Stock of Cerecor Inc. (incorporated by reference to Exhibit 3.1 to the Current Report on Form 8-K filed on December 27, 2018).
3.2	Third Amended and Restated Bylaws of Avalo Therapeutics, Inc. (incorporated by reference to Exhibit 3.2 to the Current Report on Form 8-K filed on August 26, 2021).
4.1	Second Amended and Restated Investors' Rights Agreement, dated as of July 11, 2014 (incorporated by reference to Exhibit 4.1 to the Registration Statement on Form S-1 filed on June 12, 2015).
4.2	Specimen Unit Certificate (incorporated by reference to Exhibit 4.13 to the Registration Statement on Form S-1/A filed on October 13, 2015).
4.3	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.3 to the Registration Statement on Form S-8 filed on May 20, 2016).
4.4	Form of Warrant to Purchase Shares of Series B Non-Voting Convertible Preferred Stock of Cerecor Inc. issued to Armistice Capital Master Fund Ltd. (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed on December 27, 2018).
4.5	Form of Warrant to Purchase Shares of Common Stock of Cerecor Inc. issued to Armistice Capital Master Fund Ltd. (incorporated by reference to Exhibit 4.2 to the Current Report on Form 8-K filed on December 27, 2018).
4.6	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed on January 8, 2021).
4.7	Warrant to Purchase Common Stock (Loan A) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.1 to the Current Report on Form 8-K filed on June 8, 2021).
4.8	Warrant to Purchase Common Stock (Loan B) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.2 to the Current Report on Form 8-K filed on June 8, 2021).
4.9	Warrant to Purchase Common Stock (Loan C) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.3 to the Current Report on Form 8-K filed on June 8, 2021).
4.10	Warrant to Purchase Common Stock (Loan D) issued June 4, 2021 by Cerecor, Inc. to Powerscourt Investments XXV, LP (incorporated by reference to Exhibit 4.4 to the Current Report on Form 8-K filed on June 8, 2021).
4.11	Warrant to Purchase Common Stock (Loan E) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.5 to the Current Report on Form 8-K filed on June 8, 2021).
4.12	Warrant to Purchase Common Stock (Loan F) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.6 to the Current Report on Form 8-K filed on June 8, 2021).

4.13	Warrant to Purchase Common Stock (Loan G) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.7 to the Current Report on Form 8-K filed on June 8, 2021).
4.14	Warrant to Purchase Common Stock (Loan H) issued June 4, 2021 by Cerecor, Inc. to Horizon Technology Finance Corporation (incorporated by reference to Exhibit 4.8 to the Current Report on Form 8-K filed on June 8, 2021).
4.15‡	Description of Registered Securities.
10.1 *	Exclusive Patent and Know-How License Agreement, effective as of March 19, 2013, by and between Essex Chemie AG and Cerecor Inc. (incorporated by reference to Exhibit 10.1 to the Registration Statement on Form S-1 filed on June 12, 2015).
10.2 *	Exclusive Patent and Know-How License Agreement, effective as of March 19, 2013, by and between Essex Chemie AG and Cerecor Inc. (incorporated by reference to Exhibit 10.2 to the Registration Statement on Form S-1 filed on June 12, 2015).
10.3 *	Exclusive Patent and Know-How License Agreement, effective as of February 18, 2015, by and between Eli Lilly and Company and Cerecor Inc. (incorporated by reference to Exhibit 10.3 to the Registration Statement on Form S-1 filed on June 12, 2015).
10.4 +	Form of Director Indemnification Agreement (incorporated by reference to Exhibit 10.12 to the Registration Statement on Form S-1/A filed on September 8, 2015).
10.5 ‡	Non-Employee Director Compensation Policy, amended January 24, 2022.
10.6	Non-Employee Director Compensation Policy, amended January 10, 2016 (incorporated by reference to Exhibit 10.17 to the Annual Report on Form 10-K filed on March 23, 2016).
10.7 +	Cerecor Inc. 2016 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on May 20, 2016).
10.8 *	License Agreement, dated as of September 8, 2016, by and between Cerecor Inc. and Eli Lilly and Company (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed on November 8, 2016).
10.9	Addendum to Exclusive License Agreement, dated as of October 13, 2016, by and between Cerecor Inc. and Eli Lilly and Company (incorporated by reference to Exhibit 10.1.1 to the Quarterly Report on Form 10-Q filed on November 8, 2016).
10.10	Registration Rights Agreement, dated as of April 27, 2017, by and between Cerecor, Inc. and Armistice Capital Master Fund Ltd. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on April 28, 2017).
10.11 *	License and Development Agreement, dated February 16, 2018, by and between Cerecor Inc. and Flamel Ireland Limited (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed on May 11, 2018).
10.11.1 +	Employment Agreement, dated April 19, 2018, by and between Cerecor Inc. and James A. Harrell, Jr. (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on April 27, 2018).

10.11.2 +	Amendment to Employment Agreement of James A. Harrell, Jr., dated October 14, 2019 (incorporated by reference to Exhibit 10.15.2 to the Annual Report on Form 10-K filed March 11, 2020).
10.12	Registration Rights Agreement, made and entered into as of August 20, 2018, between Cerecor Inc. and each of the several purchasers (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on August 20, 2018).
10.13	Lease dated September 14, 2018, by and between FP 540 Gaither, LLC and Cerecor Inc. (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on September 18, 2018).
10.14	Registration Rights Agreement, made and entered into as of December 27, 2018, between Cerecor, Inc. and Armistice Capital Master Fund Ltd. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on December 27, 2018).
10.15	Registration Rights Agreement, dated as of September 4, 2019, between Cerecor Inc. and Armistice Capital Master Fund Ltd. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on September 9, 2019).
10.16	Guarantee, dated as of November 1, 2019, made by Cerecor Inc. in favor of Deerfield CSF, LLC (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on November 4, 2019).
10.17	Contribution Agreement, made and entered into as of November 1, 2019, by and among Cerecor Inc., Armistice Capital Master Fund, Ltd. and Avadel US Holdings Inc. (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on November 4, 2019).
10.18	Assignment of License Agreement, dated August 8, 2019, entered into by and between Cerecor Inc., ES Therapeutics, LLC, and Armistice Capital Master Fund Ltd. (incorporated by reference to Exhibit 10.32 to the Annual Report on Form 10-K filed on March 11, 2020).
10.19	Contingent Value Rights Agreement, effective February 3, 2020, by and between Cerecor Inc. and American Stock Transfer & Trust Company, LLC (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on February 3, 2020).
10.20 +	Employment Agreement, effective February 3, 2020, by and between Cerecor Inc. and Michael F. Cola (incorporated by reference to Exhibit 10.3 to the Current Report on Form 8-K filed on February 3, 2020).
10.21 +	Employment Agreement, effective February 3, 2020, by and between Cerecor Inc. and Garry A. Neil (incorporated by reference to Exhibit 10.4 to the Current Report on Form 8-K filed on February 3, 2020).
10.22	Form of Securities Purchase Agreement, dated February 3, 2020 (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on February 4, 2020).
10.23 +	Amendment to Employment Agreement, effective March 11, 2020, by and between Cerecor Inc. and Michael F. Cola (incorporated by reference to Exhibit 10.5 to the Quarterly Report on Form 10-Q filed on May 7, 2020).
10.24	Securities Purchase Agreement, dated March 17, 2020, between Cerecor Inc. and the investor(s) named therein (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on March 18, 2020).

10.25	Registration Rights Agreement, dated March 17, 2020, between Cerecor Inc. and the investor(s) named therein (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on March 18, 2020).
10.26 *	Sponsored Research Agreement, dated as of November 12, 2014, between Medgenics Medical Israel Ltd. and The Children's Hospital of Philadelphia (previously filed as Exhibit 10.28 to Aevi's Annual Report on Form 10-K for the year ended December 31, 2014 and incorporated herein by reference).
10.27	Amendment #1 to Sponsored Research Agreement, dated December 18, 2015, by and between Medgenics Medical Israel Ltd. and the Children's Hospital of Philadelphia (previously filed as Exhibit 10.1 to Aevi's Current Report on Form 8-K filed December 22, 2015 and incorporated herein by reference).
10.28 *	License Agreement, dated as of November 12, 2014, between Medgenics Medical Israel Ltd. and The Children's Hospital of Philadelphia (previously filed as Exhibit 10.29 to Aevi's Annual Report on Form 10-K for the year ended December 31, 2014 and incorporated herein by reference).
10.29 *	License Agreement, dated as of September 9, 2015, between neuroFix, LLC and The Children's Hospital of Philadelphia (previously filed as Exhibit 10.2 to Aevi's Quarterly Report on Form 10-Q for the quarter ended September 30, 2015 and incorporated herein by reference).
10.30 *	Clinical Development and Option Agreement, by and between Medgenics, Inc. and Kyowa Hakko Kirin Co., Ltd., dated June 6, 2016 (previously filed as Exhibit 10.1 to Aevi's Quarterly Report on Form 10-Q for the quarter ended June 30, 2016 and incorporated herein by reference).
10.31 *	Amendment No. 1 to License Agreement, dated as of February 14, 2017, by and between The Children's Hospital of Philadelphia and Medgenics Medical Israel Ltd. (previously filed as Exhibit 10.1 to Aevi's Quarterly Report on Form 10-Q for the quarter ended March 31, 2017 and incorporated herein by reference).
10.32	Amendment # 2 to Sponsored Research Agreement, dated as of February 16, 2017, by and between Medgenics Medical Israel, Ltd. and the Children's Hospital of Philadelphia (previously filed as Exhibit 10.2 to Aevi's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 and incorporated herein by reference).
10.33	Amendment No. 1 to License Agreement, dated March 29, 2019, by and between neuroFix LLC and the Children's Hospital of Philadelphia (previously filed as Exhibit 10.3 to Aevi's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 and incorporated herein by reference).
10.34	Amendment No. 2 to License Agreement, dated March 29, 2019, by and between Medgenics Medical Israel Ltd. and the Children's Hospital of Philadelphia. (previously filed as Exhibit 10.4 to Aevi's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 and incorporated herein by reference).
10.35	Amendment No. 3 to Sponsored Research Agreement, dated March 29, 2019, by and between Medgenics Medical Israel Ltd. and the Children's Hospital of Philadelphia (previously filed as Exhibit 10.5 to Aevi's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 and incorporated herein by reference).
10.36	Letter Agreement, dated March 29, 2019, by and between the Company and the Children's Hospital of Philadelphia (previously filed as Exhibit 10.6 to Aevi's Quarterly Report on Form 10-Q for the quarter ended March 31, 2019 and incorporated herein by reference).

10.37 **	Exclusive License Agreement, dated as of July 15, 2019, by and between Aevi Genomic Medicine, Inc. and OSI Pharmaceuticals, LLC (previously filed as Exhibit 10.1 to Aevi's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 and incorporated herein by reference).
10.38	Amendment No. 3 to License Agreement, dated as of August 12, 2019, by and between Medgenics Medical Israel Ltd. and The Children's Hospital of Philadelphia (previously filed as Exhibit 10.3 to Aevi's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 and incorporated herein by reference).
10.39	Amendment No. 4 to Sponsored Research Agreement, dated as of August 12, 2019, by and between Medgenics Medical Israel Ltd. and The Children's Hospital of Philadelphia (previously filed as Exhibit 10.4 to Aevi's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 and incorporated herein by reference).
10.40 **	Option and License Agreement, dated as of August 6, 2019, by and between Aevi Genomic Medicine, Inc. and MedImmune Limited (previously filed as Exhibit 10.1 to Aevi's Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 and incorporated herein by reference).
10.41 **	Royalty Agreement, dated as of July 19, 2019, between and among Aevi Genomic Medicine, Inc., Michael F. Cola Joseph J. Grano, Jr., Kathleen Jane Grano, Joseph C. Grano, The Grano Children's Trust, Joseph C. Grano, trustee and LeoGroup Private Investment Access, LLC on behalf of Garry A. Neil (previously filed as Exhibit 10.2 to Aevi's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019 and incorporated herein by reference).
10.42 +	Employment Agreement, dated September 26, 2019, by and between Cerecor Inc. and Christopher Sullivan (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on April 27, 2020).
10.43 +	Letter Agreement, dated April 23, 2020, by and between Cerecor Inc. and Christopher Sullivan (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on April 27, 2020).
10.44 +	Separation Agreement, dated April 24, 2020, by and between Cerecor Inc. and Simon Pedder (incorporated by reference to Exhibit 10.3 to the Current Report on Form 8-K filed on April 27, 2020).
10.45 **	Amended and Restated Clinical Development and Option Agreement, dated May 28, 2020, by and between Aevi Genomic Medicine, LLC and Kyowa Kirin Co., Ltd., formerly known as Kyowa Kirin Co., Ltd. (incorporated by reference to Exhibit 10.28 to the Quarterly Report on Form 10-Q filed on August 6, 2020).
10.46 +	Cerecor Inc. Third Amended and Restated 2016 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on June 18, 2020).
10.47	Amendment No. 6 to License Agreement, dated as of November 13, 2020, by and between Medgenics Medical Israel Ltd. and The Children's Hospital of Philadelphia (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on November 20, 2020).
10.48	Amendment No. 6 to Sponsored Research Agreement, dated as of November 13, 2020, by and between Medgenics Medical Israel Ltd. and The Children's Hospital of Philadelphia (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on November 20, 2020).

10.49 +	Employment Agreement, dated February 10, 2021, by and between Cerecor Inc. and Schond L. Greenway (incorporated by reference to Exhibit 10.1 to the Current Report on Form 8-K filed on March 1, 2021).
10.50 +	Stock Option Agreement, dated March 1, 2021, by and between Cerecor Inc. and Schond L. Greenway (incorporated by reference to Exhibit 10.2 to the Current Report on Form 8-K filed on March 1, 2021).
10.51 +	Offer Letter, dated February 19, 2020, from Cerecor Inc. to H. Jeffrey Wilkins, M.D. (incorporated by reference to Exhibit 10.54 to the Annual Report on Form 10-K filed on March 8, 2021).
10.52 **	License Agreement, dated March 25, 2021, by and between Cerecor Inc. and Kyowa Hakko Kirin Co., Ltd (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed on May 13, 2021).
10.53 **	Exclusive Patent License Agreement, dated June 22, 2021, by and between Sanford Burnham Prebys Medical Discovery Institute and Cerecor Inc. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed on August 2, 2021).
10.54 **	Loan Agreement, dated June 4, 2021, by and between Horizon Technology Finance Corporation, Powerscourt Investments XXV, LP and Cerecor Inc. (incorporated by reference to Exhibit 10.2 to the Quarterly Report on Form 10-Q filed on August 2, 2021).
10.55 **	Amendment No.1 to Option and License Agreement, dated July 16, 2021, by and between Medimmune Limited and Aevi Genomic Medicine, LLC (incorporated by reference to Exhibit 10.3 to the Quarterly Report on Form 10-Q filed on August 2, 2021).
10.56	Cooperation Agreement, dated as of November 4, 2021, by and between Avalo Therapeutics, Inc. and Armistice Capital, LLC. (incorporated by reference to Exhibit 10.1 to the Quarterly Report on Form 10-Q filed on November 9, 2021).
21.1 ‡	List of Subsidiaries of the Registrant
23.1 ‡	Consent of Ernst & Young LLP, independent registered public accounting firm.
31.1 ‡	Certification of Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2 ‡	Certification of Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1 # ‡	Certification of Principal Executive Officer and Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.

101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File, formatted in inline XBRL (included in Exhibit 101).

---

* Confidential treatment has been requested for portions of this exhibit.

** Portions of this exhibit have been redacted in compliance with Regulation S-K Item 601(b)(10).

+ Management contract or compensatory agreement.

‡ Filed herewith.

This certification is being furnished solely to accompany this 10-K pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 16. 10-K Summary.

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities and Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Avalo Therapeutics, Inc.

/s/ Christopher Sullivan

Christopher Sullivan
Chief Financial Officer

Date: March 2, 2022

Pursuant to the requirements of the Securities and Exchange Act of 1934, this report 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/ Garry Neil, M.D. **Garry Neil, M.D.**	President and Chief Executive Officer *(Principal Executive Officer)*	March 2, 2022
/s/ Christopher Sullivan **Christopher Sullivan**	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 2, 2022
/s/ Steven Boyd **Steven Boyd**	Chairman of the Board of Directors and Director	March 2, 2022
/s/ June Almenoff, M.D., Ph.D. **June Almenoff, M.D., Ph.D.**	Director	March 2, 2022
/s/ Mitchell Chan **Mitchell Chan**	Director	March 2, 2022
/s/ Gilla Kaplan, Ph.D. **Gilla Kaplan, Ph.D.**	Director	March 2, 2022
/s/ Keith Maher, M.D. **Keith Maher, M.D.**	Director	March 2, 2022
/s/ Joseph Miller **Joseph Miller**	Director	March 2, 2022
/s/ Magnus Persson, M.D., Ph.D **Magnus Persson, M.D., Ph.D**	Director	March 2, 2022

AVALO THERAPEUTICS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Avalo Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Avalo Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity and cash flows for the years 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 at December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

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

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public 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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accounting for long-term debt

Description of the Matter

As discussed in Note 11 to the consolidated financial statements, the Company executed a $35 million Loan Agreement (the "Loan Agreement") during 2021, under which the Company borrowed $20 million at closing and borrowed an additional $15 million upon the achievement of certain predetermined milestones, which the Company met in the third quarter of 2021. In connection with the Loan Agreement, the Company issued warrants to the lenders to purchase an aggregate of 403,844 shares of the Company's common stock with an exercise price of $2.60 (the "Warrants"). Upon execution of the Loan Agreement and issuance of the Warrants, based on their individual fair values, the Company allocated the proceeds proportionately to the Loan and to the Warrants, of which $0.9 million was allocated to the equity-classified Warrants.

Auditing the Company's accounting for the Loan Agreement was complex due to the significant judgment required in evaluating the Company's identification of each instrument and feature requiring separate accounting recognition and determination of whether each should be classified as a liability or in shareholders' equity. The issuance of debt and warrants in one transaction resulted in additional complexity in the auditing of the estimated fair values of each instrument and feature.

How We Addressed the Matter in Our Audit

To test the accounting for the Loan Agreement, our procedures included, among others, obtaining and reviewing the executed Loan Agreement and the Company's related technical accounting analysis. We involved professionals with specialized skills and knowledge to assist in evaluating the Loan Agreement to determine the appropriateness of the Company's application of the relevant accounting guidance for the debt and warrants. We evaluated the Company's allocation of consideration received to the warrants and debt by recalculating the fair values and comparing to the Company's allocation for reasonableness. We also tested these individual fair values by evaluating the Company's valuation methodologies and testing significant inputs used in the valuation models. We also evaluated the Company's disclosures about matters related to the Loan Agreement.

/s/ Ernst & Young LLP
We have served as the Company's auditor since 2013.
Baltimore, Maryland
March 2, 2022

AVALO THERAPEUTICS, INC. and SUBSIDIARIES

Consolidated Balance Sheets

(In thousands, except share and per share data)

	December 31,	
	2021	2020
Assets		
Current assets:		
Cash and cash equivalents	$ 54,585	$ 18,919
Accounts receivable, net	1,060	2,177
Other receivables	3,739	2,208
Inventory, net	38	3
Prepaid expenses and other current assets	2,372	2,660
Restricted cash, current portion	51	38
Total current assets	61,845	26,005
Property and equipment, net	2,695	1,607
Other long-term asset	1,000	—
Intangible assets, net	38	1,585
Goodwill	14,409	14,409
Restricted cash, net of current portion	227	149
Total assets	$ 80,214	$ 43,755
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 3,369	$ 2,574
Accrued expenses and other current liabilities	16,519	11,310
Income taxes payable	—	—
Current liabilities of discontinued operations	—	1,341
Total current liabilities	19,888	15,225
Notes payable, net	32,833	—
Royalty obligation	2,000	2,000
Deferred tax liability, net	113	90
Other long-term liabilities	2,298	1,878
Total liabilities	57,132	19,193
Stockholders' equity:		
Common stock—$0.001 par value; 200,000,000 shares authorized at December 31, 2021 and 2020; 112,794,203 and 75,004,127 shares issued and outstanding at December 31, 2021 and 2020, respectively	113	75
Preferred stock—$0.001 par value; 5,000,000 shares authorized at December 31, 2021 and 2020; 0 and 1,257,143 shares issued and outstanding at December 31, 2021 and 2020, respectively	—	1
Additional paid-in capital	285,135	202,276
Accumulated deficit	(262,166)	(177,790)
Total stockholders' equity	23,082	24,562
Total liabilities and stockholders' equity	$ 80,214	$ 43,755

See accompanying notes to the consolidated financial statements.

AVALO THERAPEUTICS, INC. and SUBSIDIARIES

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except per share data)

	Year Ended December 31,	
	2021	2020
Revenues:		
Product revenue, net	$ 4,773	$ 6,699
License revenue	625	—
Total revenues, net	5,398	6,699
Operating expenses:		
Cost of product sales	1,491	300
Research and development	59,835	32,193
Acquired in-process research and development	—	25,549
General and administrative	21,832	17,418
Sales and marketing	2,826	2,341
Amortization expense	1,548	1,741
Total operating expenses	87,532	79,542
	(82,134)	(72,843)
Other (expense) income:		
Change in fair value of Investment in Aytu	—	5,208
Other (expense) income, net	(20)	409
Interest (expense) income, net	(2,391)	49
Total other (expense) income, net from continuing operations	(2,411)	5,666
Loss from continuing operations before income taxes	(84,545)	(67,177)
Income tax benefit	(196)	(2,793)
Loss from continuing operations	(84,349)	(64,384)
(Loss) income from discontinued operations	(27)	884
Net loss	$ (84,376)	$ (63,500)
Net (loss) income per share of common stock, basic and diluted:		
Continuing operations	$ (0.83)	$ (0.87)
Discontinued operations	0.00	0.01
Net loss per share of common stock, basic and diluted	$ (0.83)	$ (0.86)
Net (loss) income per share of preferred stock, basic and diluted:		
Continuing operations	$ (4.15)	$ (4.38)
Discontinued operations	0.00	0.06
Net loss per share of preferred stock, basic and diluted	$ (4.15)	$ (4.32)

See accompanying notes to the consolidated financial statements.

AVALO THERAPEUTICS, INC. and SUBSIDIARIES

Consolidated Statements of Changes in Stockholders' Equity

(In thousands, except share amounts)

	Common stock		Preferred Stock		Additional paid-in	Accumulated	Total stockholders'
	Shares	Amount	Shares	Amount	capital	deficit	equity
Balance, December 31, 2019	44,384,222	$ 45	2,857,143	$ 3	$ 135,238	$ (114290)	$ 20,996
Conversion of preferred stock to common stock	8,000,000	8	(1,600,000)	(2)	(6)	—	—
Issuance of shares related to Aevi Merger	3,893,361	4	—	—	15,492	—	15,496
Issuance of shares pursuant to registered direct offering, net	1,306,282	1	—	—	5,135	—	5,136
Issuance of shares pursuant to common stock private placement, net	1,951,219	2	—	—	3,886	—	3,888
Issuance of shares of common stock in underwritten public offering, net	15,180,000	15	—	—	35,413	—	35,428
Exercise of stock options and warrants	75,239	—	—	—	114	—	114
Restricted stock units vested during period	111,667	—	—	—	—	—	—
Restricted stock units withheld for taxes	(35,279)	—	—	—	(94)	—	(94)
Shares purchased through employee stock purchase plan	137,416	—	—	—	312	—	312
Stock-based compensation	—	—	—	—	6,786	—	6,786
Net loss	—	—	—	—	—	(63,500)	(63,500)
Balance, December 31, 2020	75,004,127	$ 75	1,257,143	$ 1	$ 202,276	$ (177,790)	$ 24,562
Issuance of shares of common stock and pre-funded warrants in underwritten public offering, net	13,971,889	14	—	—	37,639	—	37,653
Issuance of common stock in underwritten public offering, net	14,308,878	14	—	—	29,032	—	29,046
Issuance of common shares pursuant to ATM Program, net	2,000,000	2	—	—	5,228	—	5,230
Issuance of equity classified warrants related to venture debt financing agreement	—	—	—	—	861	—	861
Conversion of preferred stock to common stock	6,285,715	7	(1,257,143)	(1)	(5)	—	1
Exercise of stock options	580,617	1	—	—	1,566	—	1,567
Exercise of pre-funded warrants	308,697	—	—	—	—	—	—
Shares purchased through employee stock purchase plan	189,697	—	—	—	366	—	366
Restricted stock units vested during period	144,583	—	—	—	—	—	—
Stock-based compensation	—	—	—	—	8,172	—	8,172
Net loss	—	—	—	—	—	(84,376)	(84,376)
Balance, December 31, 2021	112,794,203	$ 113	—	$ —	$ 285,135	$ (262,166)	$ 23,082

See accompanying notes to the consolidated financial statements.

AVALO THERAPEUTICS, INC. and SUBSIDIARIES

Consolidated Statements of Cash Flows

(Amounts in thousands)

	Year Ended December 31,	
	2021	2020
Operating activities		
Net loss	$ (84,376)	$ (63,500)
Adjustments to reconcile net loss used in operating activities:		
Stock-based compensation	8,172	6,786
Depreciation and amortization	1,657	1,843
Accretion of debt discount	794	—
Deferred taxes	22	197
Acquired in-process research and development, including transaction costs	—	25,549
Change in fair value of Investment in Aytu	—	(5,208)
Change in value of Guarantee	—	(1,755)
Change in fair value of warrant liability and unit purchase option liability	—	(14)
Changes in assets and liabilities:		
Accounts receivable, net	1,117	(678)
Other receivables	(1,531)	(2,107)
Other long-term asset	(1,000)	—
Inventory, net	(35)	18
Prepaid expenses and other assets	287	(1,859)
Accounts payable	796	99
Income taxes payable	—	288
Accrued expenses and other liabilities, excluding lease liability	3,250	(196)
Lease liability, net	(45)	(2)
Net cash used in operating activities	(70,892)	(40,539)
Investing activities		
Proceeds from sale of Investment in Aytu, net	—	12,837
Net cash paid in merger with Aevi	—	(1,642)
Purchase of property and equipment	(113)	(63)
Net cash (used in) provided by investing activities	(113)	11,132
Financing activities		
Proceeds from issuance of common stock and pre-funded warrants in underwritten public offering, net	37,653	—
Proceeds from Notes and warrants, net of debt issuance costs paid	32,900	—
Proceeds from issuance of common stock in underwritten public offering, net	29,046	35,428
Proceeds from common stock pursuant to ATM Program, net	5,230	—
Proceeds from registered direct offering, net	—	5,136
Proceeds from sale of shares pursuant to common stock private placement, net	—	3,888
Proceeds from exercise of stock options	1,567	114
Proceeds from issuance of common stock under employee stock purchase plan	366	312
Restricted stock units withheld for taxes	—	(94)
Net cash provided by financing activities	106,762	44,784
Increase in cash, cash equivalents, and restricted cash	35,757	15,377
Cash, cash equivalents, and restricted cash at beginning of period	19,106	3,729
Cash, cash equivalents, and restricted cash at end of period	$ 54,863	$ 19,106
Supplemental disclosures of cash flow information		
Cash paid for interest	$ 1,585	$ —
Cash paid for taxes	$ —	$ 474
Supplemental disclosures of non-cash activities		
Leased asset obtained in exchange for new operating lease liability	$ 1,373	$ 376
Issuance of common stock in Aevi Merger	$ —	$ 15,496

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows:

	December 31,	
	2021	2020
Cash and cash equivalents	$ 54,585	$ 18,919
Restricted cash, current	51	38
Restricted cash, non-current	227	149
Total cash, cash equivalents and restricted cash	$ 54,863	$ 19,106

See accompanying notes to the consolidated financial statements.

1. Business

Avalo Therapeutics, Inc. (the "Company" or "Avalo") is a leading clinical-stage precision medicine company that discovers, develops, and commercializes targeted therapeutics for patients with significant unmet clinical need in immunology and rare genetic diseases. The Company has built a diverse portfolio of innovative therapies to deliver meaningful medical impact for patients in urgent need. Avalo's clinical candidates commonly have a proven mechanistic rationale, biomarkers and/or an established proof-of-concept to expedite and increase the probability of success.

In August 2021, the Company changed its corporate name change from Cerecor Inc. to Avalo Therapeutics, Inc. and merged certain wholly-owned subsidiaries into the Company to consolidate its corporate structure.

Avalo was incorporated and commenced operation in 2011 and completed its initial public offering in October 2015.

Liquidity

As of December 31, 2021, Avalo had $54.6 million in cash and cash equivalents. In 2021, the Company closed three equity offerings for net proceeds of approximately $72.0 million (see Note 12 to the consolidated financial statements for more information). In June 2021, the Company entered into a $35 million venture debt financing agreement (the "Loan Agreement") with Horizon Technology Finance Corporation ("Horizon") and Powerscourt Investments XXV, LP ("Powerscourt", together with Horizon, the "Lenders"). As of December 31, 2021, the Company had received the full $35 million. The Loan Agreement contains certain covenants and certain other specified events that could result in an event of default, which if not cured or waived, could result in the immediate acceleration of all or a substantial portion of the notes. As of the filing date of this Annual Report on Form 10-K, the Company was not aware of any breach of covenants, occurrence of material adverse change, nor had it received any notice of event of default from the Lenders (see Note 11 to the consolidated financial statements for more information).

In order to meet its cash flow needs, the Company applies a disciplined decision-making methodology as it evaluates the optimal allocation of the Company' resources between investing in the Company's existing pipeline assets and acquisitions or in-licensing of new assets. For the year ended December 31, 2021, Avalo generated a net loss of $84.4 million and negative cash flows from operations of $70.9 million. As of December 31, 2021, Avalo had an accumulated deficit of $262.2 million.

The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern; however, losses are expected to continue as the Company continues to invest in its research and development pipeline assets. The Company will require additional financing to fund its operations and to continue to execute its business strategy at least one year after the date the financial statements included herein were issued. These conditions raise substantial doubt about the Company's ability to continue as a going concern.

To mitigate these conditions and to meet the Company's capital requirements, management plans to use its current cash on hand along with some combination of the following: (i) dilutive and/or non-dilutive financings, (ii) federal and/or private grants, (iii) other out-licensing or strategic alliances/collaborations of its current pipeline assets, and (iv) out-licensing or sale of its non-core assets. If the Company raises additional funds through collaborations, strategic alliances or licensing arrangements with third parties, the Company might have to relinquish valuable rights to its technologies, future revenue streams, research programs or product candidates. Subject to limited exceptions, our venture debt financing agreement prohibits us from incurring certain additional indebtedness, making certain asset dispositions, and entering into certain mergers, acquisitions or other business combination transactions without prior consent of the Lenders. If the Company requires but is unable to obtain additional funding, the Company may be forced to make reductions in spending, delay, suspend, reduce or eliminate some or all of its planned research and development programs, or liquidate assets where possible. Due to the uncertainty regarding future financing and other potential options to raise additional funds, management has concluded that substantial doubt exists with respect to the Company's ability to continue as a going concern within one year after the date that the financial statements in this Annual Report on Form 10-K were issued.

Over the long term, the Company's ultimate ability to achieve and maintain profitability will depend on, among other things, the development, regulatory approval, and commercialization of its pipeline assets, and the potential receipt and sale of any priority review vouchers it receives.

2. Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board (the "FASB"). The consolidated financial statements have been prepared on the basis of continuity of operations, realization of assets, and the satisfaction of liabilities in the ordinary course of business. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded assets and liabilities that might be necessary should the Company be unable to continue as a going concern (see Note 1).

Principles of Consolidation

The consolidated financial statements include the accounts of Avalo Therapeutics, Inc. and its wholly-owned subsidiaries after elimination of all intercompany balances and transactions.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses, and related disclosures. On an ongoing basis, management evaluates its estimates, including estimates related to but not limited to, revenue recognition, cost of product sales, stock-based compensation, fair value measurements, cash flows used in management's going concern assessment, income taxes, goodwill, and clinical trial accruals. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

Discontinued Operations

In 2019, the Company entered into an asset purchase agreement with Aytu Bioscience, Inc. ("Aytu") to sell the Company's rights, title and interest in assets relating to its pediatric portfolio, namely Aciphex® Sprinkle™, Cefaclor for Oral Suspension, Karbinal™ ER, Flexichamber™, Poly-Vi-Flor® and Tri-Vi-Flor™ (the "Pediatric Portfolio"), as well as the corresponding commercial infrastructure consisting of the right to offer employment to Avalo's sales force and the assignment of supporting commercial contracts (the "Aytu Divestiture"). The Aytu Divestiture closed on November 1, 2019.

Upon the sale of the Pediatric Portfolio during the fourth quarter of 2019, the Pediatric Portfolio met all conditions required to be classified as discontinued operations. Therefore, the operating results of the Pediatric Portfolio (as a result of the Company's limited continued involvement) are reported as income from discontinued operations, net of tax in the accompanying consolidated financial statements for the years ended December 31, 2021 and 2020. The liabilities related to the Pediatric Portfolio are reported as liabilities of discontinued operations in the accompanying consolidated balance sheets as of December 31, 2020. For additional information, see Note 3.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less when purchased to be cash equivalents. The carrying amounts reported in the balance sheets for cash and cash equivalents are valued at cost, which approximates their fair value.

Restricted Cash

Restricted cash consists of the 2016 Employee Stock Purchase Plan (the "ESPP") deposits, credit card deposits, and security deposits for our leased corporate offices.

Accounts Receivable, net

Accounts receivable, net is comprised of amounts due from customers in the ordinary course of business. Accounts receivable are written off to net revenue when deemed uncollectible and recoveries of receivables previously written off are recorded when received.

Accounts receivable are considered to be past due if any portion of the receivable balance is outstanding for more than the payment terms negotiated with the customer. The Company generally negotiates payment terms of 60 days. The Company offers wholesale distributors a prompt payment discount, which is typically 2% as an incentive to remit payment within this timeframe. Accounts receivable are stated net of the estimated prompt pay discount.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash and cash equivalents. The Company maintains a portion of its cash and cash equivalent balances in the form of a money market account with a financial institution that management believes to be creditworthy. The Company has no financial instruments with off-balance sheet risk of loss.

Leases

The Company determines if an arrangement is a lease at inception. If an arrangement contains a lease, the Company performs a lease classification test to determine if the lease is an operating lease or a finance lease. The Company has identified two operating leases, which both serve as administrative office space. Right-of-use ("ROU") assets represent the right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Operating lease liabilities are recognized on the commencement date of the lease based on the present value of the future lease payments over the lease term and are included in other long-term liabilities and other current liabilities on the Company's consolidated balance sheet. ROU assets are valued at the initial measurement of the lease liability, plus any indirect costs or rent prepayments, and reduced by any lease incentives and any deferred lease payments. Operating ROU assets are recorded in property and equipment, net on the consolidated balance sheets and are amortized over the lease term. To determine the present value of lease payments on lease commencement, the Company uses the implicit rate when readily determinable, however, as most leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on information available at commencement date. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that it will exercise that option. Furthermore, the Company has elected the practical expedient to account for the lease and non-lease components as a single lease component for the leased property asset class. Lease expense is recognized on a straight-line basis over the life of the lease and is included within general and administrative expenses.

Property and Equipment

Property and equipment consists of computers, office equipment, furniture, ROU assets (discussed above), and leasehold improvements and is recorded at cost. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Property and equipment are depreciated on a straight-line basis over their estimated useful lives. The Company uses a life of four years for computers and software, and five years for equipment and furniture. For leasehold improvements, deprecation of the asset will begin at the date it is placed in service and the depreciable life of the leasehold improvement is the shorter of the lease term or the improvement's useful life. The Company uses the lesser of the lease term or ten years for leasehold improvements. Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is recognized.

Acquisitions

For acquisitions that meet the definition of a business under ASC 805, the Company records the acquisition using the acquisition method of accounting. All of the assets acquired, liabilities assumed, contractual contingencies, and contingent consideration, when applicable, are recorded at fair value at the acquisition date. Any excess of the purchase price over the fair value of the net assets acquired is recorded as goodwill. The application of the acquisition method of accounting requires management to make significant estimates and assumptions in the determination of the fair value of assets acquired and liabilities assumed in order to properly allocate purchase price consideration. For acquisitions that do not meet the definition of a business under ASC 805, *Business Combinations,* the Company accounts for the transaction as an asset acquisition.

Segment Information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision-making group, in making decisions on how to allocate resources and assess performance. As of December 31, 2021, the Company's chief operating decision makers was its Chief Executive Officer. The Chief Executive Officer views the Company's operations and manages the business as one operating segment. All long-lived assets of the Company reside in the United States.

Goodwill

The Company's goodwill relates to the amount that arose in connection with the Company's historical acquisitions which were accounted for as business combinations. Goodwill represents the excess of the purchase price over the fair value of the net assets acquired when accounted for using the acquisition method of accounting for business combinations. Goodwill is not amortized but is evaluated for impairment on an annual basis or more frequently if an event occurs or circumstances change that would more-likely-than-not reduce the fair value of the Company's reporting unit below its carrying amount. The Company consists of one reporting unit.

Upon disposal of a portion of a reporting unit that constitutes a business, the Company assigns goodwill based on the relative fair values of the portion of the reporting unit being disposed and the portion of the reporting unit remaining. This approach requires a determination of the fair value of both the business to be disposed of and the business (or businesses) within the reporting unit that will be retained.

Intangible Assets

Intangible assets with definite useful lives are amortized over their estimated useful lives and reviewed for impairment if certain events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Impairment losses are measured and recognized to the extent the carrying value of such assets exceeds their fair value.

Notes Payable

Notes payable are recorded on the balance sheet at carrying value, which is the gross balance (inclusive of the final payment fee for the Notes), less the unamortized debt discount and issuance costs. All fees, costs paid to the Lenders and all direct costs incurred by the Company are recognized as a debt discount and are amortized to interest expense using the effective interest method over the life of the loan.

Product Revenues, net

The Company generates substantially all of its revenue from sales of prescription drugs to its customers. The Company has identified a single product delivery performance obligation, which is the provision of prescription drugs to its customers based upon master service agreements in place with wholesaler distributors. The performance obligation is satisfied at a point in time, when control of the product has been transferred to the customer, at the time the product has been received by the customer. The Company determines the transaction price based on fixed consideration in its contractual agreements and the transaction price is allocated entirely to the performance obligation to provide pharmaceutical products. In determining the transaction price, a significant financing component does not exist because the timing from when the Company delivers product to when the customers pay for the product is less than one year and the customers do not pay for product in advance of the transfer of the product.

Revenues from sales of products are recorded net of any variable consideration for estimated allowances for returns, chargebacks, distributor fees, prompt payment discounts, government rebates, and other common gross-to-net revenue adjustments. The identified variable consideration is recorded as a reduction of revenue at the time revenues from product sales are recognized. The Company recognizes revenue only to the extent that it is probable that a significant revenue reversal will not occur in a future period.

Provisions for returns and government rebates are included within current liabilities in the consolidated balance sheet. Provisions for prompt payment discounts and distributor fees are included as a reduction to accounts receivable. Calculating these items involves estimates and judgments based on sales or invoice data, contractual terms, historical utilization rates, new information regarding changes in these programs' regulations and guidelines that would impact the amount of the actual rebates, its expectations regarding future utilization rates for these programs, and channel inventory data. These estimates may differ from actual consideration amount received and the Company will re-assess these estimates and judgments each reporting period to adjust accordingly.

Aytu, to which the Company sold its rights, title, and interests in assets relating to certain commercialized products in 2019, managed Millipred® commercial operations through August 31, 2021, pursuant to transition service agreements. In the third quarter of 2021, the Company finalized its trade and distribution channel to allow it to control third party distribution and began managing Millipred® commercial operations at that time.

Other receivables primarily relate to the amount due from Aytu within one year of December 31, 2021 for the cash collected by Aytu on behalf of Avalo for revenue generated by the sales of Millipred® from the second quarter of 2020 through the third quarter of 2021. Aytu is obligated to transfer the cash generated by such sales to Avalo. As of December 31, 2021, the Company believes the amount due from Aytu is fully collectible. See Note 4 to the consolidated financial statements for more information.

Returns and Allowances

Consistent with industry practice, the Company maintains a return policy that allows customers to return product within a specified period both prior to and, in certain cases, subsequent to the product's expiration date. The Company's return policy for sales made prior to August 31, 2021, generally allows for customers to receive credit for expired products within six months prior to expiration and within one year after expiration. The Company's return policy for sales post August 31, 2021, generally allows for customers to receive credit for expired products within thirty days prior to expiration and within ninety days after expiration. The provision for returns and allowances consists of estimates for future product returns and pricing adjustments. The primary factors considered in estimating potential product returns include:

- the shelf life or expiration date of each product;
- historical levels of expired product returns;
- external data with respect to inventory levels in the wholesale distribution channel;
- external data with respect to prescription demand for each of the Company's products; and
- the estimated returns liability to be processed by year of sale based on analysis of lot information related to actual historical returns.

License and Other Revenue

The Company recognizes revenues from collaboration, license or other research or sale arrangements when or as performance obligations are satisfied. For milestone payments, the Company assesses, at contract inception, whether the milestones are considered probable of being achieved. If it is probable that a significant revenue reversal will occur, the Company will not record revenue until the uncertainty has been resolved. Milestone payments that are contingent upon regulatory approval are not considered probable until the approvals are obtained as it is outside of the control of the Company. If it is probable that significant revenue reversal will not occur, the Company will estimate the milestone payments using the most likely amount method. The Company reassesses the milestones each reporting period to determine the probability of achievement.

Cost of Product Sales

Cost of product sales is comprised of (i) costs to acquire products sold to customers, (ii) license payments granting the Company rights to sell related products, (iii) royalty payments the Company is required to pay based on the product's net profit pursuant to its license and supply agreement and (iv) the value of any write-offs of obsolete or damaged inventory that cannot be sold.

Research and Development Costs

Research and development costs are expensed as incurred. These costs include, but are not limited to, expenses incurred under agreements with contract research organizations and investigative sites that conduct clinical trials and preclinical studies; the cost of acquiring, developing and manufacturing clinical trial materials; costs associated with preclinical activities and regulatory operations, pharmacovigilance and quality; costs and milestones associated with certain licensing agreements, and employee-related expenses, including salaries, benefits and stock-based compensation of research and development personnel.

Costs for certain development activities, such as clinical trials, are recognized based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations, or information provided to the Company by its vendors, such as clinical research organizations, with respect to their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the financial statements as prepaid or accrued research and development expense, as the case may be.

The Company is a party to license and development agreements for in-licensed R&D assets with third parties. Such agreements often contain future payment obligations such as royalties and milestone payments. The Company recognizes a liability (and related research and development expense) for each milestone if and when such milestone is probable and can be reasonably estimated. As typical in the biotechnology industry, each milestone has its own unique risks that the Company evaluates when determining the probability of achieving each milestone and the probability of success evolves over time as the programs progress and additional information is obtained. The Company considers numerous factors when evaluating whether a given milestone is probable including (but not limited to) the regulatory pathway, development plan, ability to dedicate sufficient funding to reach a given milestone and the probability of success.

Clinical Trial Expense Accruals

The Company estimates its expenses resulting from its obligations under contracts with vendors, clinical research organizations and consultants and under clinical site agreements in connection with conducting clinical trials. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. The Company's objective is to reflect the appropriate trial expenses in its financial statements by matching those expenses with the period in which services are performed and efforts are expended. The Company accounts for these expenses according to the progress of the trial as measured by subject progression and the timing of various aspects of the trial. The Company determines accrual estimates by taking into account discussions with applicable personnel and outside service providers as to the progress or state of consummation of trials, or the services completed. During the course of a clinical trial, the Company adjusts its clinical expense recognition if actual results differ from its estimates. The Company makes estimates of its accrued expenses as of each balance sheet date based on the facts and circumstances known to it at that time. The Company's clinical trial accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of the status and timing of services performed relative to the actual status and timing of services performed might vary and might result in it reporting amounts that are too high or too low for any particular period.

Acquired In-Process Research and Development Expenses

Acquired in-process research and development ("IPR&D") expense includes the initial costs of IPR&D projects, acquired directly in a transaction other than a business combination, that do not have an alternative future use.

Amortization Expense

Amortization expense includes the amortization of the Company's acquired intangible assets. Amortization expense is included within its own standalone line in operating expenses in the Company's consolidated statements of operations and comprehensive loss and therefore there is no amortization expense included in cost of product sales or sales and marketing expense.

Stock-Based Compensation

The Company applies the provisions of ASC 718, Compensation—Stock Compensation, which requires the measurement and recognition of compensation expense for all stock-based awards made to employees, including employee stock options, in the statements of operations and comprehensive loss.

For stock options issued to employees and members of the board of directors for their services, the Company estimates the grant date fair value of each option using the Black-Scholes option pricing model. The use of the Black-Scholes option pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. Additionally, the stock price on the date of grant is utilized in the Black-Scholes option pricing model. For awards subject to service-based vesting conditions, including those with a graded vesting schedule, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock options on a straight-line basis over the requisite service period, which is generally the vesting term. Forfeitures are recorded as they are incurred as opposed to being estimated at the time of grant and revised.

These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, the Company's stock-based compensation expense could be materially different in the future.

Income Taxes

The Company accounts for income taxes under the asset and liability method in accordance with ASC 740, *Income Taxes*. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases using enacted tax rates in effect for the year in which the differences are expected to affect taxable income. Deferred tax assets primarily include net operating loss ("NOL") and tax credit carryforwards, accrued expenses not currently deductible and the cumulative temporary differences related to certain research and patent costs. Certain tax attributes, including NOLs and research and development credit carryforwards, may be subject to an annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "IRC"). See Note 14 for further information. The portion of any deferred tax asset for which it is more likely than not that a tax benefit will not be realized must then be offset by recording a valuation allowance. The Company recognizes the tax benefit from an uncertain tax position only if it is more likely than not to be sustained upon examination based on the technical merits of the position.

The amount for which an exposure exists is measured as the largest amount of benefit determined on a cumulative probability basis that the Company believes is more likely than not to be realized upon ultimate settlement of the position. The Company's policy is to record interest and penalties on uncertain tax positions as income tax expense. As of December 31, 2021, the Company did not believe any material uncertain tax positions were present.

Comprehensive Loss

Comprehensive loss comprises net loss and other changes in equity that are excluded from net loss. For the years ended December 31, 2021 and 2020, the Company's net loss was equal to comprehensive loss and, accordingly, no additional disclosure is presented.

Recently Adopted Accounting Pronouncements

There have been no new accounting pronouncements made effective during fiscal 2021 that have significance, or potential significance, to our consolidated financial statements.

3. Aytu Divestiture

Overview of Sale of Pediatric Portfolio and Related Commercial Infrastructure to Aytu BioScience

On November 1, 2019, the Company closed on an asset purchase agreement to sell the Company's rights, title and interest in the Pediatric Portfolio and the corresponding commercial infrastructure to Aytu. Aytu paid consideration of $4.5 million in cash and approximately 9.8 million shares of Aytu convertible preferred stock, and assumed certain of the Company's liabilities, including the Company's payment obligations to Deerfield CSF, LLC ("Deerfield") and certain other liabilities primarily related to contingent consideration and sales returns. Steven Boyd, chief investment officer of Armistice Capital, LLC, a significant stockholder of the Company and a member of the Company's Board of Directors, served on Aytu's Board from March 2019 until August 30, 2021. The transactions and agreements between the Company and Aytu were approved in accordance with the Company's related party transaction policy.

The Pediatric Portfolio met all conditions to be classified as discontinued operations on November 1, 2019. Therefore, the accompanying consolidated financial statements for the year ended December 31, 2021 and 2020 reflect the operations, net of taxes, and related assets and liabilities of the Pediatric Portfolio as discontinued operations. Refer to the "Discontinued Operations" section below for more information, including Avalo's continuing involvement, which the Company expects to end in the second quarter of 2022.

Deerfield Guarantee

As of the closing date of the Aytu Divestiture on November 1, 2019, Aytu assumed the Company's debt obligation to Deerfield which included monthly payments of $0.1 million through January 2021, with a balloon payment of $15 million that was to be due in January 2021. Aytu also assumed the contingent consideration liability related to future royalties on Avadel Pharmaceuticals PLC's ("Avadel") pediatric products, which included minimum monthly payments of $0.1 million through February 2026. In conjunction with the closing of this transaction, the Company entered into a guarantee in favor of Deerfield, which guarantees the payment of the assumed liabilities to Deerfield, which included the debt obligation, the contingent consideration related to future royalties on Avadel's pediatric products and certain quarterly fixed obligation payments (collectively referred to as the "Guarantee").

Aytu publicly reported that it had paid the $15 million balloon payment to Deerfield before it came due in June 2020 and the fixed monthly payments to Deerfield ended in January 2021, thus satisfying the debt obligation. Aytu publicly reported that it had entered into a Waiver, Release and Consent in June 2021, pursuant to which it paid $2.8 million to Deerfield in early satisfaction of the remaining contingent consideration related to future royalties on Avadel's pediatric products. Aytu also agreed to pay the remaining fixed obligation of $3 million in six equal quarterly payments of $0.5 million over the next six quarters commencing September 30, 2021.

Avalo is required to make a payment under the Guarantee upon demand by Deerfield if all or any part of the fixed payments are not paid by Aytu when due or upon breach of a covenant. The remaining minimum fixed obligation commitments payable (as most recently publicly reported by Aytu) was $3 million as of September 30, 2021, which represents Avalo's maximum potential future payments under the Guarantee.

The fair value of the Guarantee, which relates to the Company's obligation to make future payments if Aytu defaults, was determined at the time of the Aytu Divestiture as the difference between (i) the estimated fair value of the assumed payments using Avalo's estimated cost of debt and (ii) the estimated fair value of the assumed payments using Aytu's estimated cost of debt. At each subsequent reporting period, the value of the Guarantee is determined based on the expected credit loss of the Guarantee with changes recorded in income from discontinued operations within the consolidated statements of operations and comprehensive loss. The Company concluded that the expected credit loss of the Guarantee was de minimis as of December 31, 2021 and 2020 based on considerations of Aytu's ability to meet its financial commitments including recent financings, cash position, operating cash flows and trends.

Discontinued Operations

The following tables summarizes the liabilities of the discontinued operations as of December 31, 2021 and 2020 (in thousands):

	December 31,	
	2021	2020
Accrued expenses and other current liabilities	—	1,342
Total current liabilities of discontinued operations	—	1,342

Aytu assumed sales returns of the Pediatric Portfolio made after the transaction close date related to sales prior to November 1, 2019 only to the extent such post-Closing sales returns exceed $2 million and are less than $2.8 million (in other words, Aytu assumed a maximum of $0.8 million of such returns). Therefore, Avalo is liable for future sales returns of the Pediatric Portfolio sold prior to the transaction close date in excess of the $0.8 million assumed by Aytu. The Company estimated no future returns as of December 31, 2021 on sales made prior to the transaction close date.

Changes to the Company's estimate of sales returns related to the Pediatric Portfolio is included within discontinued operations on the statement of operations and comprehensive loss and is shown within product revenue, net in the table summarizing the results of discontinued operations below. In future periods, as additional information becomes available, the Company expects to recognize expense (or a benefit) related to actual sales returns of the Pediatric Portfolio in excess (or less than) the returns reserve recorded, which will be recognized within discontinued operations. The Company expects this involvement to continue until sales returns are no longer accepted on sales of the Pediatric Portfolio made prior to November 1, 2019. Returns on these products may be accepted through the second quarter of 2022 (in line with the products' return policies).

The following table summarizes the results of discontinued operations for the year ended December 31, 2021 and 2020 (in thousands):

	Year Ended December 31,	
	2021	2020
Product revenue, net	$ 74	$ (871)
Operating expenses:		
Sales and marketing	101	—
Total operating expenses	101	—
Other income:		
Change in value of Guarantee	—	1,755
Total other income	—	1,755
(Loss) income from discontinued operations	$ (27)	$ 884

There were no non-cash operating items from discontinued operations for the year ended December 31, 2021 and no non-cash investing items from the discontinued operations for the year ended December 31, 2021 and 2020. The significant non-cash operating item from the discontinued operations for the year ended December 31, 2020 is contained below (in thousands):

	Year Ended December 31,	
	2021	2020
Change in value of Guarantee	—	(1,755)

4. Revenue

The Company generates substantially all of its revenue from sales of Millipred®, an oral prednisolone indicated across a wide variety of inflammatory conditions, which is considered a prescription drug. The Company sells its prescription drug in the United States primarily through wholesale distributors. Wholesale distributors account for substantially all of the Company's net product revenues and trade receivables. For the year ended December 31, 2021, the Company's three largest customers accounted for approximately 63%, 21%, and 16% of the Company's total net product revenues. For the year ended December 31, 2020, the Company's three largest customers accounted for approximately 46%, 25%, and 27% of the Company's total net product revenues. Revenue from sales of prescription drugs was $4.8 million and $6.7 million for the years ended December 31, 2021 and 2020, respectively.

The Company has a license and supply agreement for the Millipred® product with a wholly owned subsidiary of Teva Pharmaceutical Industries Ltd. ("Teva"), which expires on September 30, 2023. Beginning July 1, 2021, Avalo is required to pay Teva fifty percent of the net profit of the Millipred® product following each calendar quarter, subject to a $0.5 million quarterly minimum payment. For the year ended December 31, 2021, the Company recognized $1.0 million in cost of product sales related to the royalty. Dr. Sol Barer served as the Chairman of the Company's board of directors until June 2021 and currently serves as the Chairman of Teva's board of directors.

Aytu managed Millipred® commercial operations until August 31, 2021 pursuant to transition service agreements, which included managing the third-party logistics provider and providing accounting reporting services. Aytu collected cash on behalf of Avalo for revenue generated by sales of Millipred® from the second quarter of 2020 through the third quarter of 2021 and is obligated to transfer the cash generated by such sales to Avalo. In the third quarter of 2021, Avalo finalized its trade and distribution channel to allow it to control third party distribution and began managing Millipred® commercial operations at that time. The current transition services agreement allows Aytu to withhold cash of $2 million until September 30, 2022 and $1 million until December 2024. As of December 31, 2021, the total receivable balance was estimated to be approximately $4.3 million, $1 million of which was recognized in other long-term assets and the remainder recognized in other receivables. Subsequent to December 31, 2021, the Company received $2.2 million from Aytu.

License revenue was $0.6 million for the year ended December 31, 2021, which was related to upfront fees received in the second quarter of 2021 as a result of the out-license and assignment, respectively, of the Company's rights to its non-core neurology pipeline assets, AVTX-301 and AVTX-406 to Alto Neurosciences, Inc. ("Alto") and ES Therapeutics, LLC ("ES"), respectively. ES is a wholly-owned subsidiary of Armistice Capital Master Fund Ltd. (an affiliate of Armistice Capital, LLC and collectively "Armistice"), which is a significant stockholder of the Company and whose chief investment officer, Steven Boyd, and managing director, Keith Maher, serve on the Company's Board of Directors. The transaction with ES was approved in accordance with the Company's related party transaction policy. Avalo is eligible to receive additional payments upon achievement of specified development, regulatory and sales-based milestones for both AVTX-301 and AVTX-406 and is also eligible to royalty payments based on net sales of AVTX-301; refer to Note 15 for more information.

5. Net Loss Per Share

The Company computes earnings per share ("EPS") using the two-class method. The two-class method of computing EPS is an earnings allocation formula that determines EPS for common stock and any participating securities according to dividends declared and participation rights in undistributed earnings.

The Company had two classes of stock outstanding during the year ended December 31, 2021; common stock and preferred stock. The convertible preferred stock outstanding during the period converted to shares of common stock on a 1-for-5 ratio and had the same rights, preferences, and privileges as common stock other than it held no voting rights. In April 2021, Armistice converted the remaining 1,257,143 shares of convertible preferred stock into 6,285,715 shares of Avalo's common stock (refer to Note 11 for more information).

Under the two-class method, the convertible preferred stock was considered a separate class of stock until the time it was converted to common shares for EPS purposes and therefore basic and diluted EPS is provided below for both common stock and preferred stock for the years ended December 31, 2021 and 2020.

EPS for common stock and EPS for preferred stock is computed by dividing the sum of distributed earnings and undistributed earnings for each class of stock by the weighted average number of shares outstanding for each class of stock for the period. In applying the two-class method, undistributed earnings are allocated to common stock and preferred stock based on the weighted average shares outstanding during the period, which assumes the convertible preferred stock has been converted to common stock. The weighted average number of common shares outstanding as of December 31, 2021 includes the weighted average effect of the pre-funded warrants issued in connection with the underwritten public offering that closed in January 2021, the exercise of which requires nominal consideration for the delivery of the shares of common stock (refer to Note 11 for more information).

Diluted net (loss) income per share includes the potential dilutive effect of common stock equivalents as if such securities were converted or exercised during the period, when the effect is dilutive. Common stock equivalents include: (i) outstanding stock options and restricted stock units, which are included under the "treasury stock method" when dilutive; and (ii) common stock to be issued upon the exercise of outstanding warrants, which are included under the "treasury stock method" when dilutive. Because the impact of these items is generally anti-dilutive during periods of net loss, there is no difference between basic and diluted loss per common share for periods with net losses. In periods of net loss, losses are allocated to the participating security only if the security has not only the right to participate in earnings, but also a contractual obligation to share in the Company's losses.

The following tables set forth the computation of basic and diluted net (loss) income per share of common stock for and preferred stock for the years ended December 31, 2021 and 2020 (in thousands, except per share amounts):

	Year Ended December 31, 2021			
	Common stock		Preferred Stock	
	Continuing Operations	Discontinued Operations	Continuing Operations	Discontinued Operations
Numerator:				
Allocation of undistributed net (loss) income	$ (82,849)	$ (27)	$ (1,500)	$ —
Denominator:				
Weighted average shares	99,888,447	99,888,447	361,644	361,644
Basic and diluted net (loss) income per share	$ (0.83)	$ 0.00	$ (4.15)	$ 0.00

	Year Ended December 31, 2020			
	Common stock		Preferred Stock	
	Continuing Operations	Discontinued Operations	Continuing Operations	Discontinued Operations
Numerator:				
Allocation of undistributed net (loss) income	$ (58,440)	$ 802	$ (5,944)	$ 82
Denominator:				
Weighted average shares	66,688,464	66,688,464	1,356,597	1,356,597
Basic and diluted net (loss) income per share	$ (0.87)	$ 0.01	$ (4.38)	$ 0.06

The following outstanding securities at December 31, 2021 and 2020 have been excluded from the computation of diluted weighted shares outstanding, as they could have been anti-dilutive:

	December 31,	
	2021	2020
Stock options	13,650,978	9,830,674
Warrants on common stock[1]	4,406,224	4,002,380
Restricted Stock Units	11,250	155,833

[1] *The weighted average number of common shares outstanding as of December 31, 2021 includes the weighted average effect of the 1,676,923 pre-funded warrants issued in connection with the underwritten public offering that closed in January 2021 because the exercise of such warrants requires nominal consideration ($0.001 per share exercise price for each pre-funded warrant). 308,880 of the pre-funded warrants have been exercised. Therefore, the 1,368,043 pre-funded warrants outstanding as of December 31, 2021 are not included in the table above.*

6. Asset Acquisition

Aevi Merger

In the first quarter of 2020, the Company consummated its merger with Aevi Genomic Medicine Inc. ("Aevi"), in which Avalo acquired the rights to AVTX-002, AVTX-006 and AVTX-007 (the "Merger" or the "Aevi Merger").

The Merger consideration included (i) stock valued at approximately $15.5 million, resulting in the issuance of approximately 3.9 million shares of Avalo common stock to Aevi stockholders, (ii) forgiveness of $4.1 million the Company had loaned Aevi prior to the Merger closing, (iii) contingent value rights for up to an additional $6.5 million in subsequent payments based on certain development milestones (discussed further in Note 14), and (iv) transaction costs of $1.5 million.

The Company recorded this transaction as an asset purchase as opposed to a business combination because management concluded that substantially all the value received was related to one group of similar identifiable assets, which was the in-process research and development ("IPR&D") for two early phase therapies. The Company considered these pipeline assets similar due to similarities in the risks of development, stage of development, regulatory pathway, patient populations and economics of commercialization. The fair value of $25.5 million (consisting primarily of $24 million IPR&D, $0.3 million of cash and $0.9 million of assembled workforce) was immediately recognized as acquired in-process research and development expense in the Company's consolidated statement of operations and comprehensive loss because the IPR&D asset has no alternate use due to the stage of development. The assembled workforce asset was recorded to intangible assets and will be amortized over an estimated useful life of two years.

7. Fair Value Measurements

ASC No. 820, *Fair Value Measurements and Disclosures* ("ASC 820") defines fair value as the price that would be received to sell an asset, or paid to transfer a liability, in the principal or most advantageous market in an orderly transaction between market participants on the measurement date. The fair value standard also establishes a three-level hierarchy, which requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. The valuation hierarchy is based upon the transparency of inputs to the valuation of an asset or liability on the measurement date. The three levels are defined as follows:

- Level 1—inputs to the valuation methodology are quoted prices (unadjusted) for an identical asset or liability in an active market.
- Level 2—inputs to the valuation methodology include quoted prices for a similar asset or liability in an active market or model-derived valuations in which all significant inputs are observable for substantially the full term of the asset or liability.
- Level 3—inputs to the valuation methodology are unobservable and significant to the fair value measurement of the asset or liability.

The following table presents, for each of the fair value hierarchy levels required under ASC 820, the Company's assets and liabilities that are measured at fair value on a recurring basis (in thousands):

	December 31, 2021 Fair Value Measurements Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 54,010	$ —	$ —

	December 31, 2020 Fair Value Measurements Using		
	Quoted prices in active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
Assets			
Investments in money market funds*	$ 17,503	$ —	$ —

**Investments in money market funds are reflected in cash and cash equivalents on the accompanying consolidated balance sheets.*

As of December 31, 2021 and 2020, the Company's financial instruments included cash and cash equivalents, restricted cash, accounts receivable, other receivables, prepaid and other current assets, accounts payable, accrued expenses and other current liabilities, and long term-debt. The carrying amounts reported in the accompanying consolidated financial statements for cash and cash equivalents, restricted cash, accounts receivable, other receivables, prepaid and other current assets, accounts payable, and accrued expenses and other current liabilities approximate their respective fair values because of the short-term nature of these accounts. The estimated fair value of the Company's debt approximates its carrying value as of December 31, 2021 and is in Level Two of the fair value hierarchy (refer to Note 10 for more information).

No changes in valuation techniques or inputs occurred during the years ended December 31, 2021 and 2020. No transfers of assets between Level 1 and Level 2 of the fair value measurement hierarchy occurred during the years ended December 31, 2021 and 2020.

8. Property and Equipment

Property and equipment as of December 31, 2021 and 2020 consisted of the following (in thousands):

	December 31,	
	2021	2020
Furniture and equipment	$ 185	$ 153
Computers and software	56	56
Right-of-use assets	2,001	918
Leasehold improvements	739	657
Total property and equipment	2,981	1,784
Less accumulated depreciation	(286)	(177)
Property and equipment, net	$ 2,695	$ 1,607

Depreciation expense was $0.1 million for the years ended December 31, 2021 and December 31, 2020.

Leases

The Company currently occupies two leased properties, both of which serve as administrative office space. The Company determined that both leases are operating leases based on the lease classification test performed at lease commencement.

The annual base rent for the Company's office located in Rockville, Maryland is $0.2 million, subject to annual 2.5% increases over the term of the lease. The lease provided for a rent abatement for a period of 12 months following the Company's date of occupancy. The lease has an initial term of ten years from the date the Company makes its first annual fixed rent payment, which occurred in January 2020. The Company has the option to extend the lease two times, each for a period of five years, and may terminate the lease as of the sixth anniversary of the first annual fixed rent payment, upon the payment of a termination fee.

The Company subleased additional administrative office space in Chesterbrook, Pennsylvania with an annual base rent of $0.3 million through November 2021. The Company subsequently entered into a lease for administrative office space in Chesterbook Pennsylvania that commenced on December 1, 2021 (the "New Chesterbrook Lease"). The annual base rent for the New Chesterbrook Lease is $0.2 million and the annual operating expenses are approximately $0.1 million. The annual base rent is subject to periodic increases of approximately 2.4% over the term of the lease. The lease provides for a rent abatement period of 3 months following lease commencement. The lease has an initial term of 5.25 years from the lease commencement.

The weighted average remaining term of the operating leases at December 31, 2021 was 6.5 years.

Supplemental balance sheet information related to the leased properties include (in thousands):

	As of	
	December 31, 2021	December 31, 2020
Property and equipment, net	$ 2,001	$ 918
Accrued expenses and other current liabilities	$ 485	$ 426
Other long-term liabilities	2,018	1,038
Total operating lease liabilities	$ 2,503	$ 1,464

The operating lease ROU assets are included in property and equipment and the lease liabilities are included in accrued expenses and other current liabilities and other long-term liabilities in the Company's consolidated balance sheets. The Company utilized a weighted average discount rate of 9.2% to determine the present value of the lease payments.

The components of lease expense for the years ended December 31, 2021 and 2020 were as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Operating lease cost*	$ 393	$ 345

**Includes short-term leases, which are immaterial.*

The following table shows a maturity analysis of the operating lease liability as of December 31, 2021 (in thousands):

	Undiscounted Cash Flows
2022	$ 485
2023	528
2024	537
2025	547
2026	557
Thereafter	683
Total lease payments	$ 3,337
Less implied interest	(834)
Total	$ 2,503

9. Goodwill and Intangible Assets

There were no changes in the carrying amount of goodwill for the years ended December 31, 2021 and 2020.

The changes in intangible assets for the years ended December 31, 2021 and 2020 were as follows (in thousands):

Balance as of December 31, 2019	$ 2,426
Additions	900
Amortization	(1,741)
Balance as of December 31, 2020	$ 1,585
Amortization	(1,547)
Balance as of December 31, 2021	$ 38

As a result of the asset acquisition accounting treatment of the Aevi Merger, the Company recognized an assembled workforce intangible asset of $0.9 million during the first quarter of 2020, which was assigned a two-year useful life and will be fully amortized in 2022.

The following is a summary of intangible assets held by the Company at December 31, 2021 and 2020, respectively (in thousands):

	December 31, 2021			
	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount	Weighted-Average Remaining Life
				(in years)
Acquired Product Marketing Rights	$ 5,056	$ (5,056)	$ —	0.0
Acquired Assembled Workforce	900	(862)	38	0.1
Total	$ 5,956	$ (5,918)	$ 38	0.1

	December 31, 2020			
	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount	Weighted-Average Remaining Life
				(in years)
Acquired Product Marketing Rights	$ 5,056	$ (3,950)	$ 1,106	0.9
Acquired Assembled Workforce	1,050	(571)	479	1.1
Total	$ 6,106	$ (4,521)	$ 1,585	0.9

10. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities as of December 31, 2021 and 2020 consisted of the following (in thousands):

	December 31,	
	2021	2020
Research and development	$ 8,221	$ 4,939
Compensation and benefits	4,310	3,120
General and administrative	1,275	771
Sales and marketing	111	31
Commercial operations	1,733	1,913
Royalty payment	375	—
Lease liability, current	485	426
Other	9	110
Total accrued expenses and other current liabilities	$ 16,519	$ 11,310

11. Notes Payable

Overview

On June 4, 2021, the Company entered into a $35 million Loan Agreement with the Lenders. In accordance with the Loan Agreement, $20 million was funded on the closing date (the "Initial Note"), with the remaining $15 million fundable upon the Company achieving certain predetermined milestones, which the Company met in the third quarter of 2021. On July 30, 2021, after achieving a predetermined milestone, the Company borrowed $10 million, which was evidenced by a second note payable (the "Second Note"). On September 29, 2021, after achieving a second predetermined milestone, the Company borrowed the remaining $5 million, which was evidenced by a third note payable (the "Third Note", and collectively with the Initial and Second Notes, the "Notes").

Each advance under the Loan Agreement will mature 42 months from the first day of the month following the funding of the advance. Each advance accrues interest at a per annum rate of interest equal to 6.25% plus the prime rate, as reported in the Wall Street Journal (subject to a floor of 3.25%). The Loan Agreement provided for interest-only payments for each advance for the first 18 months, however the interest-only period was extended to 24 months as a result of the Company satisfying the Interest Only Extension

Milestone (as defined in the Loan Agreement) in the third quarter of 2021. Thereafter, amortization payments will be payable in monthly installments of principal and interest through each advance's maturity date. Upon ten business days' prior written notice, the Company may prepay all of the outstanding advances by paying the entire principal balance and all accrued and unpaid interest, subject to prepayment charges of up to 3% of the then outstanding principal balance. Upon the earlier of (i) payment in full of the principal balance, (ii) an event of default, or (iii) the maturity date, the Company will pay an additional final payment of 3% of the principal loan amount to the Lenders.

Each advance of the loan is secured by a lien on substantially all of the assets of the Company, other than Intellectual Property and Excluded Collateral (in each case as defined in the Loan Agreement), and contains customary covenants and representations, including a financial reporting covenant and limitations on dividends, indebtedness, collateral, investments, distributions, transfers, mergers or acquisitions taxes, corporate changes, deposit accounts, and subsidiaries.

The events of default under the Loan Agreement include but are not limited to, failing to make a payment, breach of covenant, or occurrence of a material adverse change. If an event of default occurs, the Lenders are entitled to accelerate the payment of the loan obligations to be due immediately or take other enforcement actions. The accelerated payment obligations would include the outstanding principal balance (inclusive of the 3% final payment fee), a prepayment charge on the outstanding principal balance of up to 3%, and any accrued and unpaid interest. As of the filing date of this Annual Report on Form 10-K, the Company was not aware of any breach of covenants, occurrence of material adverse change, nor had it received any notice of event of default from the Lenders.

On June 4, 2021, pursuant to the Loan Agreement, the Company issued warrants to the Lenders to purchase an aggregate of 403,844 shares of the Company's common stock with an exercise price of $2.60 (the "Warrants"). The Warrants are exercisable for ten years from the date of issuance. The Lenders may exercise the Warrants either by (a) cash or check or (b) through a net issuance conversion. The Warrants, which met equity classification, were recognized as a component of permanent stockholders' equity within additional paid-in-capital and were recorded at the issuance date using a relative fair value allocation method. The Company valued the Warrants at issuance, which resulted in a discount on the debt, and allocated the proceeds from the loan proportionately to the Notes and to the Warrants, of which $0.9 million was allocated to the Warrants.

For the year ended December 31, 2021, the Company incurred $2.1 million in debt issuance costs, including legal fees in connection with the Loan Agreement, fees paid directly to the lender, and other direct costs. All fees, warrants, and costs paid to the Lenders and all direct costs incurred by the Company are recognized as a debt discount and are amortized to interest expense using the effective interest method over the term of the loan. The $1.1 million final payment fee is included in the contractual cash flows and is accreted to interest expense using the effective interest method over the term of the loan.

The effective interest rate of the Notes, including the accretion of the final payment, was 13.5% as of December 31, 2021.

Balance sheet information related to the note payable for the Notes is as follows (in thousands):

	As of December 31,		
	2021	2020	Maturity
Initial Note	20,600	—	January 2025
Second Note	10,300	—	February 2025
Third Note	5,150	—	April 2025
Notes payable, gross[1]	36,050	—	
Less: Unamortized debt discount and issuance costs	3,217	—	
Carrying value of notes payable, non-current	$ 32,833	$ —	

[1] *Balance includes $1.1 million final payment fee for the Notes, which represents 3% of the principal loan amount.*

As of December 31, 2021, the estimated future principal payments due on the Notes were as follows (in thousands):

	As of December 31, 2021
2022	—
2023	10,278
2024	23,333
2025	2,439
2026	—
Total[1]	$ 36,050

[1] *Total principal payment balance includes $1.1 million final payment fee for the Notes, which represents 3% of the principal loan amount.*

12. Capital Structure

Pursuant to the Company's amended and restated certificate of incorporation, the Company is authorized to issue two classes of stock; common stock and preferred stock. At December 31, 2021, the total number of shares of capital stock the Company was authorized to issue was 205,000,000 of which 200,000,000 was common stock and 5,000,000 was preferred stock. All shares of common and preferred stock have a par value of $0.001 per share.

Common Stock

2021 Financings

Q3 2021 Equity Financing

On September 17, 2021, the Company closed an underwritten public offering of 14,308,878 shares of its common stock for net proceeds of $29.0 million. Armistice participated in the offering by purchasing 5,454,545 shares of common stock, on the same terms as all other investors. Certain affiliates of Nantahala Capital Management LLC (collectively, "Nantahala"), which beneficially owned greater than 5% of the Company's outstanding common stock at the time of the offering, participated in the offering on the same terms as all other investors.

At-the-Market Offering Program

In July 2021, the Company entered into an "at-the-market" sales agreement with Cantor Fitzgerald & Co. and RBC Capital Markets, LLC (together, the "Agents"), pursuant to which the Company may sell from time to time, shares of its common stock having an aggregate offering price of up to $50 million through the Agents. In August 2021, the Company sold 2 million shares of common stock under the ATM Program for net proceeds of approximately $5.2 million.

Debt Financing

As part of the Loan Agreement entered into in the second quarter of 2021, on June 4, 2021, the Company issued the Warrants to Horizon and Powerscourt to purchase an aggregate of 403,844 shares of the Company's common stock with an exercise price of $2.60. The Warrants are exercisable for ten years from the date of issuance. Refer to Note 11 for additional information.

Q1 2021 Equity Financing

In January 2021, the Company closed an underwritten public offering of 13,971,889 shares of its common stock and 1,676,923 pre-funded warrants for net proceeds of $37.7 million. Armistice participated in the offering by purchasing 2,500,000 shares of common stock, on the same terms as all other investors. Nantahala participated in the offering by purchasing 1,400,000 shares of common stock, on the same terms as all other investors.

Nantahala also purchased pre-funded warrants to purchase up to 1,676,923 shares of common stock at a purchase price of $2.599, which represents the per share public offering price for the common stock less the $0.001 per share exercise price for each pre-funded warrant.

The pre-funded warrants are exercisable at any time after their original issuance at the option of the holder, in the holder's discretion, by (i) payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise or (ii) a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. The holder will not be entitled to exercise any portion of any pre-funded warrant if the holder's ownership of the Company's common stock would exceed 9.99% following such exercise.

In the event of certain fundamental transactions, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind of amounts of securities, cash or other property that the holders would have received had it exercised the pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercise contained in the pre-funded warrants.

The pre-funded warrants were classified as a component of permanent stockholders' equity within additional paid-in capital and were recorded at the issuance date using a relative fair value allocation method. The pre-funded warrants are equity classified because they (i) are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, (ii) are immediately exercisable, (iii) do not embody an obligation for the Company to repurchase its shares, (iv) permit the holder to receive a fixed number of shares of common stock upon exercise, (v) are indexed to the Company's common stock and (vi) meet the equity classification criteria. In addition, such pre-funded warrants do not provide any guarantee of value or return. The Company valued the pre-funded warrants at issuance, concluding that their sales price approximated their fair value, and allocated net proceeds from the sale proportionately to the common stock and pre-funded warrants, of which $4.4 million was allocated to the pre-funded warrants and recorded as a component of additional paid-in capital.

In the fourth quarter of 2021, 308,880 of the pre-funded warrants were exercised resulting in the issuance of 308,697 shares of common stock. As of December 31, 2021, 1,368,043 pre-funded warrants remain outstanding.

2020 Financings

On June 11, 2020, the Company closed an underwritten public offering of 15,180,000 shares of its common stock for net proceeds of approximately $35.4 million. Armistice participated in the offering by purchasing 2,000,000 shares of common stock on the same terms as all other investors. Additionally, certain of the Company's officers participated in the offering by purchasing an aggregate of 110,000 shares of common stock, on the same terms as all other investors.

On March 17, 2020, the Company entered into a securities purchase agreement with Armistice pursuant to which the Company sold 1,951,219 shares of the Company's common stock for net proceeds of approximately $3.9 million.

On February 6, 2020, the Company closed a registered direct offering with certain institutional investors for the sale by the Company of 1,306,282 shares of the Company's common stock for net proceeds of approximately $5.1 million. Armistice participated in the offering by purchasing 1,256,282 shares of common stock from the Company, on the same terms as all other investors.

Aevi Merger

On February 3, 2020, under the terms of the Aevi Merger noted above in Note 5, the Company issued approximately 3.9 million shares of common stock.

Common Stock Warrants

At December 31, 2021, the following common stock warrants were outstanding:

Number of common shares underlying warrants	Exercise price per share	Expiration date
2,380	$ 8.68	May 2022
4,000,000	$ 12.50	June 2024
1,368,043	$ 0.001	—
403,844	$ 2.60	June 2031
5,774,267		

Convertible Preferred Stock

On December 26, 2018, the Company filed a Certificate of Designation of Preferences of Series B Non-Voting Convertible Preferred Stock ("Series B Convertible Preferred Stock" or "convertible preferred stock") of Avalo Therapeutics, Inc. (the "Certificate of Designation of the Series B Preferred Stock") classifying and designating the rights, preferences and privileges of the Series B Convertible Preferred Stock. The Certificate of Designation of the Series B Convertible Preferred Stock authorized 2,857,143 shares of convertible preferred stock. The Series B Convertible Preferred Stock converted to shares of common stock on a 1-for-5 ratio and had the same rights, preferences, and privileges as common stock other than it held no voting rights. During the first quarter of 2020, the sole holder of the Series B Preferred Stock, Armistice converted 1,600,000 shares of the convertible preferred stock into 8,000,000 shares of Avalo's common stock. In April 2021, Armistice converted the remaining 1,257,143 shares of Series B Convertible Preferred Stock into 6,285,715 shares of Avalo's common stock. As of December 31, 2021, the Company had no preferred stock outstanding.

13. Stock-Based Compensation

2016 Equity Incentive Plan

On April 5, 2016, the Company's board of directors adopted the 2016 Equity Incentive Plan (the "2016 Plan") as the successor to the 2015 Omnibus Plan (the "2015 Plan"). The 2016 Plan was approved by the Company's stockholders and became effective on May 18, 2016 (the "2016 Plan Effective Date"). Upon the 2016 Plan Effective Date, the 2016 Plan reserved and authorized up to 600,000 additional shares of common stock for issuance, as well as 464,476 unallocated shares remaining available for grant of new awards under the 2015 Plan. An Amended and Restated 2016 Equity Incentive Plan was approved by the Company's stockholders in May 2018, which increased the share reserve by an additional 1.4 million shares. A Second Amended and Restated 2016 Equity Incentive Plan was approved by the Company's stockholders in August 2019, which increased the share reserve by an additional 850,000 shares. A Third Amended and Restated Equity Incentive Plan (the "2016 Third Amended Plan") was approved by the Company's stockholders in June 2020 which increased the share reserve by an additional 2,014,400 shares. During the term of the 2016 Third Amended Plan, the share reserve will automatically increase on the first trading day in January of each calendar year ending on (and including) January 1, 2026, by an amount equal to 4% of the total number of outstanding shares of common stock of the Company on the last trading day in December of the prior calendar year. As of December 31, 2021, there were 1,570,867 shares available for future issuance under the 2016 Third Amended Plan. On January 1, 2022, pursuant to the terms of the 2016 Third Amended Plan an additional 4,511,768 shares were made available for issuance.

Option grants expire after ten years. Employee options typically vest over three or four years. Employees typically receive a new hire option grant, as well as an annual grant in the first or second quarter of each year. Options granted to directors typically vest immediately or over a period of one or three years. Directors may elect to receive stock options in lieu of board compensation, which vest immediately. For stock options granted to employees and non-employee directors, the estimated grant date fair market value of the Company's stock-based awards is amortized ratably over the individuals' service periods, which is the period in which the awards vest. Stock-based compensation expense includes expense related to stock options, restricted stock units and employee stock purchase plan shares. The amount of stock-based compensation expense recognized for the years ended December 31, 2021 and 2020 was as follows (in thousands):

	Year Ended December 31,	
	2021	2020
Research and development	$ 1,775	$ 1,340
General and administrative	5,983	5,131
Sales and marketing	414	315
Total stock-based compensation	$ 8,172	$ 6,786

In June 2021, the Company's former Chairman of the Board resigned from the Board. The Company and the former Chairman subsequently entered into an agreement for him to serve as a strategic advisor to the Board and the Company, including serving on the Company's Scientific Advisory Board, for a period of at least one year. As consideration for these services, the Company modified his outstanding stock option awards to allow them to continue to vest during the term during which he serves as an advisor. Additionally, the outstanding options were amended to extend the exercisability period. As a result of the modification, in the second quarter of 2021, the Company recognized $1.4 million of compensation cost within general and administrative expenses, $1 million of which related to options with market-based vesting conditions (which were fully vested prior to the modification) and $0.4 million of which

related to options with service-based vesting conditions. At December 31, 2021, there was $0.1 million of unrecognized compensation cost related to the modification of service-based options that will be recognized over a weighted-average period of 0.5 years.

Stock options with service-based vesting conditions

The Company has granted stock options that contain service-based vesting conditions. The compensation cost for these options is recognized on a straight-line basis over the vesting periods. The following table summarizes the Company's service-based option activity for the year ended December 31, 2021:

	Options Outstanding			
	Number of shares	Weighted average exercise price per share	Weighted average grant date fair value per share	Weighted average remaining contractual term (in years)
Balance at December 31, 2020	8,830,674	$ 3.95	$ 2.36	7.7
Granted	5,336,173	$ 3.18	$ 2.13	
Exercised	(580,617)	$ 2.70	$ 1.74	
Forfeited	(567,758)	$ 3.41	$ 2.54	
Expired	(367,494)	$ 4.47	$ 3.74	
Balance at December 31, 2021	12,650,978	$ 3.69	$ 2.29	8.1
Exercisable at December 31, 2021	5,106,090	$ 4.11	$ 2.37	7.0

In March 2021, the Company granted its then newly appointed Chief Financial Officer options with service-based vesting conditions to purchase 0.5 million shares of common stock as an inducement option grant, pursuant to NASDAQ Listing Rule 5635(c)(4). In January 2021, the Company granted 2.7 million options with service-based vesting conditions to its employees as part of its annual stock option award. Additionally, throughout 2021, the Company granted options with service-based vesting conditions to new employees who started with the Company during the year.

Our former Chief Executive Officer, who was separated from the Company in February 2022, entered into an amended employment agreement in March 2020 in which his base salary in cash was reduced to an annual rate of $35,568 (the “Reduction”), which represents the minimum exempt annual salary. In consideration for the Reduction, on a quarterly basis, the Company granted stock options, which vested immediately, for the purchase of a number of shares of the Company’s common stock with a total value (based on the Black-Scholes valuation methodology) based on a pro rata total annual value of the foregone salary (the “Salary Option”). If the closing stock price per share was below $2.07 on the grant date, then the Salary Option was not granted and instead the former CEO receives compensation in cash for the given quarter. For the year ended December 31, 2021, the foregone cash salary, and therefore the fair value granted in stock options, was $464,432.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company’s common stock for those stock options that had exercise prices lower than the fair value of the Company’s common stock. As of December 31, 2021, the aggregate intrinsic value of options outstanding was $0.2 million. The aggregate intrinsic value of options currently exercisable as of December 31, 2021 was $0.2 million. The aggregate intrinsic value of options exercised for the years ended December 31, 2021 and 2020 was $0.5 million and $0.1 million, respectively. There were 3,147,750 options that vested during the year ended December 31, 2021 with a weighted average exercise price of $3.60 per share. The total grant date fair value of shares which vested during the year ended December 31, 2021 and 2020 was $7 million and $3.3 million, respectively.

The Company recognized stock-based compensation expense of $6.8 million related to stock options with service-based vesting conditions for the year ended December 31, 2021. At December 31, 2021, there was $13.6 million of total unrecognized compensation cost related to unvested service-based vesting conditions awards. This unrecognized compensation cost is expected to be recognized over a weighted-average period of 2.6 years.

Stock options with market-based vesting conditions

The Company granted stock options that contained market-based vesting conditions. As of December 31, 2021, all market-based vesting conditions had been satisfied. The following table summarizes the Company's market-based option activity for the year ended December 31, 2021 (in thousands, except for share amounts):

	Options Outstanding			
	Number of shares	Weighted average exercise price per share	Weighted average remaining contractual term (in years)	Aggregate intrinsic value (1)
Balance at December 31, 2020	1,000,000	$ 3.29	9.5	$ 65
Granted	—	$ —		
Balance at December 31, 2021	1,000,000	$ 3.29	2.5	$ —
Exercisable at December 31, 2021	1,000,000	$ 3.29	2.5	$ —

(1) The aggregate intrinsic value in the above table represents the total pre-tax amount that a participant would receive if the option had been exercised on the last day of the respective fiscal period. Options with a market value less than its exercise value are not included in the intrinsic value amount.

The Company recognized stock-based compensation expense of $1.1 million related to stock options with market-based vesting conditions for the year ended December 31, 2021.

Stock-based compensation assumptions

The following table shows the assumptions used to compute stock-based compensation expense for stock options with service-based vesting conditions granted under the Black-Scholes valuation model for the years ended December 31, 2021 and 2020 and the assumptions used to compute stock-based compensation expense for market-based stock option grants under a Monte Carlo simulation for the year ended December 31, 2020:

	Year Ended December 31,					
Service-based options	2021			2020		
Expected term of options (in years)	0.76	—	6.25	1.75	—	6.25
Expected stock price volatility	73.0%	—	86.5%	69.9%	—	79.0%
Risk-free interest rate	0.07%	—	1.34%	0.19%	—	1.48%
Expected annual dividend yield	0%			0%		
Market-based options						
Expected term of options (in years)				4.3	—	5.0
Expected stock price volatility				80.0%		
Risk-free interest rate				0.30%		0.34%
Expected annual dividend yield				0%		

The valuation assumptions were determined as follows:

- Expected term of options: Due to lack of sufficient historical data, the Company estimates the expected life of its stock options with service-based vesting granted to employees and members of the board of directors as the arithmetic average of the vesting term and the original contractual term of the option for service-based options.

- Expected stock price volatility: The Company estimated the expected volatility based on a blend of Avalo's actual historical volatility of its stock price and the historical volatility of other similar publicly-traded biotechnology companies. The Company calculated the historical volatility of the selected companies by using weekly closing prices over a period of the expected term of the associated award. The companies were selected based on their risk profiles, enterprise value, position within the industry, and historical share price information sufficient to meet the expected term of the associated award. A decrease in the selected volatility would decrease the fair value of the underlying instrument.

- Risk-free interest rate: The Company bases the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected option term.

- Expected annual dividend yield: The Company estimated the expected dividend yield based on consideration of its historical dividend experience and future dividend expectations. The Company has not historically declared or paid dividends to stockholders. Moreover, it does not intend to pay dividends in the future, but instead expects to retain any earnings to invest in the continued growth of the business. Accordingly, the Company assumed an expected dividend yield of 0%.

Restricted Stock Units

The Company measures the fair value of the restricted stock units using the stock price on the date of the grant. The restricted shares typically vest annually over a four-year period beginning on the first anniversary of the award. The following table summarizes the Company's RSU activity for the year ended December 31, 2021:

	RSUs Outstanding	
	Number of shares	Weighted average grant date fair value
Unvested RSUs at December 31, 2020	155,833	$ 4.91
Vested	(144,583)	$ 4.94
Unvested RSUs at December 31, 2021	11,250	$ 4.50

Employee Stock Purchase Plan

On April 5, 2016, the Company's board of directors approved the ESPP. The ESPP was approved by the Company's stockholders and became effective on May 18, 2016 (the "ESPP Effective Date").

Under the ESPP, eligible employees can purchase common stock through accumulated payroll deductions at such times as are established by the administrator. The ESPP is administered by the compensation committee of the Company's board of directors. Under the ESPP, eligible employees may purchase stock at 85% of the lower of the fair market value of a share of the Company's common stock (i) on the first day of an offering period or (ii) on the purchase date. Eligible employees may contribute up to 15% of their earnings during the offering period. The Company's board of directors may establish a maximum number of shares of the Company's common stock that may be purchased by any participant, or all participants in the aggregate, during each offering or offering period. Under the ESPP, a participant may not accrue rights to purchase more than $25,000 of the fair market value of the Company's common stock for each calendar year in which such right is outstanding.

Upon the ESPP Effective Date, the Company reserved and authorized up to 500,000 shares of common stock for issuance under the ESPP. On January 1 of each calendar year, the aggregate number of shares that may be issued under the ESPP automatically increases by a number equal to the lesser of (i) 1% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, and (ii) 500,000 shares of the Company's common stock, or (iii) a number of shares of the Company's common stock as determined by the Company's board of directors or compensation committee. As of December 31, 2021, 1,735,611 shares remained available for issuance. On January 1, 2022, the number of shares available for issuance under the ESPP increased by 500,000.

In accordance with the guidance in ASC 718-50, *Employee Share Purchase Plans*, the ability to purchase shares of the Company's common stock at the lower of the offering date price or the purchase date price represents an option and, therefore, the ESPP is a compensatory plan under this guidance. Accordingly, stock-based compensation expense is determined based on the option's grant-date fair value and is recognized over the requisite service period of the option. The Company used the Black-Scholes valuation model and recognized stock-based compensation expense of $0.3 million for the years ended December 31, 2021 and December 31, 2020.

Subsequent Equity Grants

On January 4, 2022, the Company granted its newly appointed Chief Commercial Officer, Stephen Smolinski, options to purchase 0.4 million shares of common stock at an exercise price of $1.70 per share as an inducement option grant, pursuant to NASDAQ Listing Rule 5635(c)(4). The options will vest over four years, with one-quarter of such options vesting on the first anniversary of the grant date and the remaining three-quarters of the options vesting in equal monthly installments over the following 36 months, in each case, subject to continued employment with the Company through the applicable vesting date.

In the first quarter of 2022, pursuant to Dr. Neil's letter agreement in connection with his promotion to CEO, the Company will grant a stock option to Dr. Garry Neil to purchase 1 million shares of the Company's common stock. Additionally, in the first quarter of 2022, pursuant to Mr. Sullivan's letter agreement in connection with his promotion to CFO, the Company will grant a stock option to Mr. Christopher Sullivan to purchase 400,000 shares of the Company's common stock. The stock options will vest over four years, with one-quarter of such options vesting on the first anniversary of the grant date and the remaining three-quarters of the options vesting in equal monthly installments over the following 36 months, in each case, subject to continued employment with the Company through the applicable vesting date.

14. Income Taxes

The Company accounts for income taxes in accordance with ASC 740, *Income Taxes*. ASC 740 is an asset and liability approach that requires the recognition of deferred tax assets and liabilities for the expected tax consequences or events that have been recognized in our financial statement or tax returns. ASC 740 also clarifies the accounting for uncertainty in income taxes recognized in the financial statement. The interpretation prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken, or expected to be taken, in a tax return. There were no significant matters determined to be unrecognized tax benefits taken or expected to be taken in a tax return that have been recorded in our financial statement for the year ended December 31, 2021. Tax years beginning in 2018 are generally subject to examination by taxing authorities, although net operating losses from all years are subject to examinations and adjustments for at least three years following the year in which the attributes are used.

ASC 740 provides guidance on the recognition of interest and penalties related to income taxes. There were no interest or penalties related to uncertain tax positions arising in the years ended December 31, 2021 and 2020. It is the Company's policy to treat interest and penalties, to the extent they arise, as a component of income taxes.

The income tax provision from continuing operations consisted of the following for the years ending December 31, 2021 and 2020 (in thousands):

	December 31,	
	2021	2020
Current:		
Federal	$ (219)	$ (2,158)
State	1	(439)
Total Current	(218)	(2,597)
Deferred:		
Federal	24	(147)
State	(2)	(49)
Total Deferred	22	(196)
Net income tax benefit	$ (196)	$ (2,793)

The net deferred tax liabilities consisted of the following for the years ending December 31, 2021 and 2020 (in thousands):

	December 31,	
	2021	2020
Deferred tax assets (liabilities):		
Net operating losses	$ 31,816	$ 14,935
Tax credits	4,871	2,748
Stock-based compensation	3,080	2,849
Accrued compensation	965	893
Installment sale	445	462
Other reserves	381	543
Lease liability	590	358
Prepaid expenses	(353)	(247)
Right-of-use asset	(472)	(224)
Basis difference in tangible and intangible assets, net	2,020	1,935
Total deferred tax assets, net	43,343	24,252
Less valuation allowance	(43,456)	(24,343)
Net deferred taxes	$ (113)	$ (91)

As of December 31, 2021, the Company has roughly $134.2 million of gross net operating losses for federal and state tax purposes that will begin to expire in 2031, including $131.7 million of gross NOLs for federal and conforming states that carry forward indefinitely. As of December 31, 2021, the Company has various research tax credits of $4.9 million that will begin to expire in 2038.

The income tax benefit (expense) for the years ended December 31, 2021 and 2020 differed from the amounts computed by applying the U.S. federal income tax rate of 21% as follows:

	December 31,	
	2021	2020
Federal statutory rate	21.00 %	21.00 %
Stock compensation	(1.48)	(0.47)
State taxes	—	0.60
Research and development credit	2.52	2.53
Acquired in-process research and development	—	(8.09)
NOL carryback due to CARES Act	0.26	3.26
Other	(0.15)	(0.16)
Valuation allowance	(21.93)	(14.46)
Effective income tax rate	0.22 %	4.21 %

The valuation allowance recorded by the Company as of December 31, 2021 and 2020 resulted from the uncertainties of the future utilization of deferred tax assets mainly resulting from net operating loss carry forwards for federal and state income tax purposes as well as the federal research and experimental and orphan drug tax credits. In assessing the realization of deferred tax assets, management considers the reversal of deferred tax liabilities, as well as whether it is more likely than not that all or some portion of the deferred tax assets will not be realized. The ultimate realization of the deferred tax assets is dependent upon generation of future taxable income during the periods in which temporary differences are expected to reverse. The Company has established deferred tax liabilities for indefinite lived intangible assets consisting of goodwill that are not amortized for financial reporting purposes, but are tax deductible and therefore amortized over 15 years for tax purposes. The Company has concluded that the resulting deferred tax liability will also have an indefinite life unless there is an impairment of the related assets (for financial reporting purposes), or the disposal of the business to which the assets relate. Losses generated in years after 2017 will also have an indefinite life and will be available to offset 80 percent of any federal tax liability and will be available to offset many of the state deferred tax liabilities subject to utilization limits. A portion of existing deferred tax assets will reverse in the future, potentially generating net operating losses that will also be available to offset a portion of the indefinite lived deferred tax liability. Based on the consideration of these facts, the Company concluded it is more likely than not that a significant portion of its remaining gross deferred tax assets less the reversal of

deferred tax liabilities will not be realized in the future, accordingly, a full valuation allowance continues to be recorded against the Company's deferred tax asset as of December 31, 2021 and December 31, 2020.

The Company will continue to assess and evaluate strategies that will enable the deferred tax asset, or portion thereof, to be utilized, and will reduce the valuation allowance appropriately as such time when it is determined that the "more likely than not" criteria is satisfied.

Sections 382 and 383 of the Internal Revenue Code of 1986 subject the future utilization of net operating losses and certain other tax attributes, such as research and experimental tax credits, to an annual limitation in the event of certain ownership changes, as defined. The Company has undergone an ownership change study through June 2020 and has determined that a "change in ownership" as defined by IRC Section 382 of the Internal Revenue Code of 1986, as amended, and the rules and regulations promulgated thereunder, did occur in February 2012, July 2014, and April 2017. Based on the Company having undergone multiple ownership changes throughout their history, these NOLs will free up at varying rates each year. Subsequent to the changes in ownership previously listed, the NOL and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period. This could limit the amount of NOLs and research and development credits that the Company can utilize annually to offset future taxable income or tax liabilities. The Company has not analyzed the historical or potential impact of its equity financings on beneficial ownership after June 30, 2020 and therefore no determination has been made whether the entire NOL carryforward balance are subject to any additional Internal Revenue Code Section 382 limitation. To the extent there is a limitation, which could be significant, there would be a reduction in the deferred tax asset with an offsetting reduction in the valuation allowance. Subsequent ownership changes may further affect the limitation in future years. All of the Company's tax years are currently open to examination by each tax jurisdiction in which the Company is subject to taxation.

In March 2020, the Coronavirus Aid, Relief and Economic Security Act (the "CARES Act") was signed into law, which provided a number of tax provisions. In particular, the CARES Act included temporary changes regarding the utilization and five year carry back of losses generated in 2018, 2019 and 2020, temporary changes regarding interest deductions, technical corrections from prior tax legislation related to qualified improvement property, and various other measures. The ability for the Company to carry back a portion of its 2018 loss to the 2017 tax year resulted in a refund claim of $2.6 million, which was reflected as a benefit in 2020. The Company received its federal refund in 2021 and recorded an additional benefit of $0.2 million in 2021 related to additional interest received.

15. Commitments and Contingencies

Litigation

Litigation – General

The Company may become party to various contractual disputes, litigation, and potential claims arising in the ordinary course of business. The Company currently does not believe that the resolution of such matters will have a material adverse effect on its financial position or results of operations except as otherwise disclosed in this report.

Karbinal Royalty Make-Whole Provision

In 2018, in connection with the acquisition of Avadel's pediatric products, the Company entered into a supply and distribution agreement (the "Karbinal Agreement") with TRIS Pharma Inc. ("TRIS"). As part of the Karbinal Agreement, the Company had an annual minimum sales commitment, which is based on a commercial year that runs from August 1 through July 31, of 70,000 units through 2025. The Company was required to pay TRIS a royalty make whole payment ("Make-Whole Payments") of $30 for each unit under the 70,000 units annual minimum sales commitment through 2025.

As a part of the Aytu Divestiture, which closed on November 1, 2019, the Company assigned all payment obligations, including the Make-Whole Payments, under the Karbinal Agreement (collectively, the "TRIS Obligations") to Aytu. However, under the original license agreement, the Company could ultimately be liable for the TRIS Obligations to the extent Aytu fails to make the required payments. The future Make-Whole Payments to be made by Aytu are unknown as the amount owed to TRIS is dependent on the number of units sold.

Possible Future Milestone Payments for In-Licensed Compounds

General

The Company is a party to license and development agreements with various third parties, which contain future payment obligations such as royalties and milestone payments (discussed further below). The Company recognizes a liability (and related expense) for each milestone if and when such milestone is probable and can be reasonably estimated. As typical in the biotechnology industry, each milestone has its own unique risks that the Company evaluates when determining the probability of achieving each milestone and the probability of success evolves over time as the programs progress and additional information is obtained. The Company considers numerous factors when evaluating whether a given milestone is probable including (but not limited to) the regulatory pathway, development plan, ability to dedicate sufficient funding to reach a given milestone and the probability of success.

AVTX-002 KKC License Agreement

On March 25, 2021, the Company entered into a license agreement with Kyowa Kirin Co., Ltd. ("KKC") for exclusive worldwide rights to develop, manufacture and commercialize AVTX-002, KKC's first-in-class fully human anti-LIGHT (TNFSF14) monoclonal antibody for all indications (the "KKC License Agreement"). The KKC License Agreement replaced the Amended and Restated Clinical Development and Option Agreement between the Company and KKC dated May 28, 2020.

Under the KKC License Agreement, the Company paid KKC an upfront license fee of $10 million. The Company is also required to pay KKC up to an aggregate of $112.5 million based on the achievement of specified development and regulatory milestones. Upon commercialization, the Company is required to pay KKC sales-based milestones aggregating up to $75 million tied to the achievement of annual net sales targets.

Additionally, the Company is required to pay KKC royalties during a country-by-country royalty term equal to a mid-teen percentage of annual net sales. The Company is required to pay KKC a double-digit percentage (less than 30%) of the payments that the Company receives from sublicensing of its rights under the KKC License Agreement, subject to certain exclusions. Avalo is responsible for the development and commercialization of AVTX-002 in all indications worldwide (other than the option in the KKC License Agreement that, upon exercise by KKC, allows KKC to develop, manufacture and commercialize AVTX-002 in Japan).

The Company recognized the upfront license fee of $10 million within research and development expenses for the year ended December 31, 2021 and made the payment in April 2021. There has been no cumulative expense recognized as of December 31, 2021 related to the milestones under the KKC License Agreement. The Company will continue to monitor the milestones at each reporting period.

AVTX-006 Astellas License Agreement

The Company has an exclusive license agreement with OSI Pharmaceuticals, LLC, an indirect wholly owned subsidiary of Astellas Pharma, Inc. ("Astellas"), for the worldwide development and commercialization of the novel, second generation mTORC1/2 inhibitor (AVTX-006). Under the terms of the license agreement, there was an upfront license fee of $0.5 million. The Company is required to pay Astellas up to an aggregate of $5.5 million based on the achievement of specified development and regulatory milestones. The Company is also required to pay Astellas a tiered mid-to-high single digit percentage of the payments that Avalo receives from sublicensing of its rights under the Astellas license agreement, subject to certain exclusions. Upon commercialization, the Company is required to pay Astellas royalties during a country-by-country royalty term equal to a tiered mid-to-high single digit percentage of annual net sales. Avalo is fully responsible for the development and commercialization of the program.

For the year ended December 31, 2021, the Company recognized a $0.5 million development milestone payment within research and development expenses. There has been $0.5 million of cumulative expense recognized as of December 31, 2021 related to the milestones under this license agreement. The Company will continue to monitor the remaining milestones at each reporting period.

AVTX-007 AstraZeneca License Agreement

The Company has an exclusive global license with Medimmune Limited, a subsidiary of AstraZeneca plc ("AstraZeneca"), to develop and commercialize a fully human, anti-IL-18 monoclonal antibody (AVTX-007). Under the terms of the license agreement, there was an upfront license fee of $6 million in cash and equity. The Company is required to pay AstraZeneca up to an aggregate of $71.5 million based on the achievement of certain development and regulatory milestones. Upon commercialization, the Company is required to pay AstraZeneca sales-based milestone payments aggregating up to $90 million tied to the achievement of annual net sales targets. Additionally, the Company is also required to pay AstraZeneca royalties during a country-by-country royalty term equal to a

tiered low double-digit percentage of annual net sales. Avalo is fully responsible for the development and commercialization of the program.

No expense related to this license agreement was recognized in the year ended December 31, 2021. There has been $1.5 million of cumulative expense recognized as of December 31, 2021 related to the milestones under this license agreement. The Company will continue to monitor the remaining milestones at each reporting period.

AVTX-008 Sanford Burnham Prebys License Agreement

On June 22, 2021, the Company entered into an Exclusive Patent License Agreement with Sanford Burnham Prebys Medical Discovery Institute (the "Sanford Burnham Prebys License Agreement") under which the Company obtained an exclusive license to a portfolio of issued patents and patent applications covering an immune checkpoint program (AVTX-008).

Under the terms of the Sanford Burnham Prebys License Agreement, the Company incurred an upfront license fee of $0.4 million, as well as patent costs of $0.5 million. The Company is required to pay Sanford Burnham Prebys up to an aggregate of $24.2 million based on achievement of specified development and regulatory milestones. Upon commercialization, the Company is required to pay Sanford Burnham Prebys sales-based milestone payments aggregating up to $50.0 million tied to annual net sales targets. Additionally, the Company is required to pay Sanford Burnham Prebys royalties during a country-by-country royalty term equal to a low-to-mid single digit percentage of annual net sales. The Company is also required to pay Sanford Burnham Prebys a tiered low-double digit percentage of the payments that Avalo receives from sublicensing of its rights under the Sanford Burnham Prebys License Agreement, subject to certain exclusions. Avalo is fully responsible for the development and commercialization of the program.

The Company recognized the upfront license fee of $0.4 million within research and development expenses and the upfront patent expense of $0.5 million within general and administrative expenses for the year December 31, 2021. There has been no cumulative expense recognized as of December 31, 2021 related to the milestones under this license agreement. The Company will continue to monitor the milestones at each reporting period.

Possible Future Milestone Proceeds for Out-Licensed Compounds

AVTX-301 Out-License

On May 28, 2021, the Company out-licensed its rights in respect of its non-core asset, AVTX-301, to Alto Neuroscience, Inc. ("Alto"). The Company initially in-licensed the compound from an affiliate of Merck & Co., Inc. in 2013.

Under the out-license agreement, the Company received a mid-six-digit upfront payment from Alto. The Company is also eligible to receive up to an aggregate of $18.6 million based on the achievement of specified development, regulatory and commercial sale milestones. Additionally, the Company is entitled to a less than single digit percentage royalty based on annual net sales. Alto is fully responsible for the development and commercialization of the program.

Avalo recognized the upfront fee as license revenue for the year ended December 31, 2021. The Company has not recognized any milestones as of December 31, 2021.

AVTX-406 License Assignment

On June 9, 2021, the Company assigned its rights, title, interest, and obligations under an in-license covering its non-core asset, AVTX-406, to ES, a wholly-owned subsidiary of Armistice. The transaction with ES was approved in accordance with Avalo's related party transaction policy.

Under the assignment agreement, the Company received a low-six-digit upfront payment from ES. The Company is also eligible to receive up to an aggregate of $6 million based on the achievement of specified development and regulatory milestones. Upon commercialization, the Company is eligible to receive sales-based milestone payments aggregating up to $20 million tied to annual net sales targets. ES is fully responsible for the development and commercialization of the program.

Avalo recognized the upfront fee as license revenue for the year ended December 31, 2021. The Company has not recognized any milestones as of December 31, 2021.

AVTX-501 Sale to Janssen

In August 2017, the Company sold its worldwide rights to AVTX-501 to Janssen Pharmaceuticals, Inc. ("Janssen") in exchange for initial gross proceeds of $25 million. The Company is also eligible to receive up to an aggregate of $20 million based on the achievement of specified development and regulatory milestones. Janssen is fully responsible for the development and commercialization of the program.

The Company has not recognized any milestones as of December 31, 2021.

AVTX-611 License Assignment

In August 2019, the Company assigned its rights, title, interest, and obligations under an in-license covering its non-core asset, AVTX-611, to ES, a wholly-owned subsidiary of Armistice.

Upon commercialization, the Company is eligible to receive sales-based milestone payments aggregating up to $20 million tied to annual net sales targets. ES is fully responsible for the development and commercialization of the program.

The Company has not recognized any milestones as of December 31, 2021.

Related Party and Acquisition Related Contingent Liabilities

AVTX-006 Royalty Agreement with Certain Related Parties

In July 2019, Aevi entered into a royalty agreement, and liabilities thereunder were assumed by the Company upon closing of its merger with Aevi, where certain investors, including LeoGroup Private Investment Access, LLC on behalf of Garry Neil, the Company's Chief Executive Officer, and Mike Cola, the Company's former Chief Executive Officer (collectively, the "Investors"), in exchange for a one-time aggregate payment of $2 million (the "Royalty Agreement"). Collectively, the Investors will be entitled to an aggregate amount equal to a low-single digit percentage of the aggregate net sales of Astellas' second generation mTORC1/2 inhibitor, AVTX-006. At any time beginning three years after the date of the first public launch of AVTX-006, Avalo may exercise, at its sole discretion, a buyout option that terminates any further obligations under the Royalty Agreement in exchange for a payment to Investors of an aggregate of 75% of the net present value of the royalty payments. A majority of the independent members of the board of directors and the audit committee of Aevi approved the Royalty Agreement.

Avalo assumed this Royalty Agreement upon closing of the Aevi Merger and it is recorded as a royalty obligation within the Company's accompanying consolidated balance sheet as of December 31, 2021. Because there is a significant related party relationship between the Company and the Investors, the Company has treated its obligation to make royalty payments under the Royalty Agreement as an implicit obligation to repay the funds advanced by the Investors. As the Company makes royalty payments in accordance with the Royalty Agreement, it will reduce the liability balance. At the time that such royalty payments become probable and estimable, and if such amounts exceed the liability balance, the Company will impute interest accordingly on a prospective basis based on such estimates, which will result in a corresponding increase in the liability balance.

Aevi Merger Possible Future Milestone Payments

A portion of the consideration for the Aevi Merger includes two future contingent development milestones worth up to an additional $6.5 million. All milestones are payable in either shares of the Company's common stock or cash, at the election of the Company.

The first milestone was the enrollment of a patient in a Phase 2 study related to AVTX-002 for use in pediatric onset Crohn's disease, AVTX-006 (any indication), or AVTX-007 (any indication) prior to February 3, 2022, which would have resulted in a milestone payment of $2 million. The Company did not meet the first milestone prior to February 3, 2022 and it was not probable that the milestone would be met as of December 31, 2021. Therefore, no contingent consideration related to this milestone was recognized as of December 31, 2021 and no future contingent consideration will be recognized.

The second milestone is the receipt of an NDA approval for either AVTX-006 or AVTX-007 from the FDA on or prior to February 3, 2025. If this milestone is met, the Company is required to make a milestone payment of $4.5 million.

The contingent consideration related to the second development milestone will be recognized if and when such milestone is probable and can be reasonably estimated. As of the consummation of the Merger on February 3, 2020 and as of December 31, 2021, no contingent consideration related to the second development milestone has been recognized. The Company will continue to monitor the second milestone at each reporting period.

Ichorion Asset Acquisition Possible Future Milestone Payments

In September 2018, the Company acquired Ichorion Therapeutics, Inc., which included the acquisition of three compounds for inherited metabolic disorders known as CDGs (AVTX-801, AVTX-802 and AVTX-803) and one other preclinical compound. Consideration for the transaction included shares of Avalo common stock and three future contingent development milestones for the acquired compounds worth up to an additional $15 million. All milestones are payable in either shares of the Company's common stock or cash, at the election of the Company.

The first and second milestone were marketing approval of the first and second product, respectively, by the FDA on or prior to December 31, 2021. The Company did not meet the first or second milestone as of December 31, 2021. The Company would have been required to make a $6 million and $5 million milestone payment, respectively, if the first and the second milestone were met. As a result, no contingent consideration related to these milestones were recognized as of December 31, 2021 and no future contingent consideration will be recognized.

The third milestone is marketing approval of a protide molecule by the FDA on or prior to December 31, 2023. If this milestone is met, the Company is required to make a milestone payment of $4 million.

The contingent consideration related to the third development milestone will be recognized if and when such milestone is probable and can be reasonably estimated. No contingent consideration related to the third milestone has been recognized as of December 31, 2021. The Company will continue to monitor the third development milestone at each reporting period.

16. Subsequent Events

In the first quarter of 2022, the Company separated from certain section 16 officers. Each of the former officers are entitled to the benefits provided in their respective separation agreements. The severance related to their terminations, which includes base salary and bonuses earned in 2022 prior to their separations, is approximately $1.6 million and will be recognized as a liability in the first quarter of 2022. Additionally, the separated executive’s stock options were modified to accelerate the vesting of certain awards and extend the exercisability periods. The Company will evaluate the financial statement impact of the stock compensation modifications in the first quarter of 2022.

CORPORATE INFORMATION

Directors

Steven Boyd, *Chairman of the Board*
Chief Investment Officer, Armistice Capital, LLC

June Almenoff, M.D., Ph.D.
Chief Medical Officer, Redhill Biopharma Ltd.

Mitchell Chan
Operating Partner, Catalio Capital Management, LP

Gilla Kaplan, Ph.D.
Chief Research Officer, Gilrose Pharmaceuticals, Inc.

Keith Maher, M.D.
Managing Director, Armistice Capital, LLC

Joseph Miller
Chief Financial Officer, Aurinia Pharmaceuticals Inc.

Magnus Persson, M.D., Ph.D.
Founding Partner and Chairman of the Board, Eir Ventures Partners AB
Associate Professor in Physiology, Karolinska Institutet
Pediatrician, Barnsjukhuset Martina, Stockholm

Officers

Garry Neil, M.D., *President and Chief Executive Officer*

Christopher Sullivan, *Chief Financial Officer*

Headquarters

540 Gaither Road, Suite 400
Rockville, Maryland 20850
(410) 522-8707

Transfer Agent

American Stock Transfer & Trust Company, LLC
6201 15th Avenue
Brooklyn, New York 11219
(718) 921-8200

Website

www.avalotx.com

Stock Listing

Avalo Therapeutics, Inc.'s common stock is listed on the Nasdaq Capital Market and quoted under the symbol "AVTX."

540 Gaither Road, Suite 400
Rockville, Maryland 20850
Phone: (410) 522-8707
www.avalotx.com