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, 2019.

OR

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

For the transition period from to

Commission file number 001-38898

Applied Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**81-3405262**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
545 Fifth Avenue, Suite 1400, New York, NY	**10017**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code **(212)-220-9226**

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 par value	**APLT**	The Nasdaq Global Market

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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 Rule 12b-2 of the Exchange Act.

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

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

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

The approximate aggregate market value of voting stock held by non-affiliates of the registrant, based upon the last sale price of the registrant's common stock on the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2019 , as reported on the NASDAQ Global Market, was approximately $68,000,000. This calculation excludes approximately 8,800,000 shares held by directors, executive officers and 10% or greater shareholders of the registrant. Exclusion of these shares does not constitute a determination that each such person is an affiliate of the registrant.

As of March 12, 2020, the total number of shares outstanding of the registrant's Common Stock was 21,969,277 shares, net of treasury shares.

Documents Incorporated by Reference:

Portions of the registrant's definitive proxy statement for the registrant's 2020 annual meeting, to be filed within 120 days after the the close of the registrant's fiscal year, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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PART I

CAUTIONARY NOTE REGARDING FORWARD- LOOKING STATEMENTS

This Annual Report on Form 10-K may contain “forward-looking statements” within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “predict,” “positioned,” “potential,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled “Risk Factors” in this Annual Report on Form 10-K:

- our plans to develop and commercialize our product candidates;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our ability to take advantage of expedited regulatory pathways for any of our product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to successfully acquire or license additional product candidates on reasonable terms;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to obtain regulatory approval of our current and future product candidates;
- our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business and product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations and liabilities thereunder;

- developments relating to our competitors and our industry; and
- other factors that may impact our financial results

The foregoing list of risks is not exhaustive. Other sections of this Annual Report on Form 10-K may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report on Form 10-K, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the sections titled “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

ITEM 1. BUSINESS.

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against validated molecular targets in indications of high unmet medical need. We focus on molecules and pathways whose role in the disease process is well known based on prior research, but have previously failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development leverages recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on abbreviated regulatory pathways. Our first molecular target is aldose reductase, or AR, an enzyme that converts glucose to sorbitol under oxidative stress conditions, and is implicated in multiple diseases. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. The detrimental consequences of aberrant AR activation have been well established by decades of prior research. Our AR inhibitor, or ARI, program currently includes three small molecules, which are all designed to be potent and selective ARIs, and are engineered to have unique tissue permeability profiles to target different disease states, including diabetic complications, heart disease and a rare pediatric metabolic disease. Applying our strategy from our ARI program, we have also developed a program targeting selective inhibition of phosphatidylinositol 3-kinase, or PI3K, subunits that has resulted in an early-stage oncology pipeline. The result of this unique multifaceted approach to drug development is a portfolio of highly specific and selective product candidates that we believe are significantly de-risked and can move quickly through the development process.

Our lead product candidate, AT-007, is a novel central nervous system, or CNS, penetrant ARI that we are developing for the treatment of galactosemia, a devastating rare pediatric metabolic disease that affects how the body processes a simple sugar called galactose, and for which there is no known cure or approved treatment available. High levels of galactose circulating in the blood and tissues of galactosemia patients enable AR to convert galactose to a toxic metabolite, galactitol, which results in long-term complications ranging from CNS dysfunction to cataracts. We have demonstrated in an animal model of galactosemia that treatment with AT-007 reduces toxic galactitol levels and prevents disease complications. We believe that galactosemia may qualify for accelerated approval, as well as for the rare pediatric disease priority review voucher, or RPD-PRV, program. Additionally, the U.S. Food and Drug Administration, or FDA, recently released draft guidance for industry on drug development for low prevalence, slowly progressing rare metabolic diseases, for which we believe galactosemia qualifies. The guidance allows for a biomarker-based development program if clinical efficacy and a link to a relevant biomarker can be demonstrated in an

animal model of disease. We received Orphan Designation for AT-007 in galactosemia in May 2019. In June 2019 we initiated a pivotal Phase 1/2 clinical study in healthy volunteers and adults with galactosemia examining safety, pharmacokinetics and biomarker effects of AT-007. In healthy volunteers, AT-007 was found to be well tolerated at all doses tested (5mg/kg to 20mg/kg) and pharmacokinetics were compatible with once daily oral dosing.

The study is a double-blind placebo-controlled trial evaluating safety and pharmacokinetics of AT-007 in healthy volunteers, as well as safety, pharmacokinetics and biomarker effects in adult galactosemia patients over 28 days of once daily oral dosing. The key biomarker outcome of the study was reduction in galactitol, an aberrant toxic metabolite of galactose, formed by AR in galactosemia patients.

In January 2020, we announced positive topline results. AT-007 treatment resulted in a statistically significant and robust reduction in plasma galactitol versus placebo in adult galactosemia patients. Reductions in galactitol were dose dependent, with higher concentrations of AT-007 resulting in a greater magnitude of reduction in galactitol. At the highest dose tested (20mg/kg), AT-007 significantly reduced plasma galactitol 45-54% from baseline versus placebo (with a p value of less than 0.01). Galactitol reduction was rapid and sustained over time. No substantial change from baseline was observed in placebo treated patients. AT-007 was well tolerated, with no drug-related adverse events noted to date in galactosemia patients or in the 72 healthy volunteers treated in Part 1 of the trial.

We will continue to characterize AT-007 long-term safety in adult galactosemia patients and intend to initiate a pediatric study.

Our second product candidate, AT-001, is a novel ARI with broad systemic exposure and peripheral nerve permeability that we are developing for the treatment of diabetic cardiomyopathy, or DbCM, a fatal fibrosis of the heart. We are also developing AT-001 for diabetic peripheral neuropathy, or DPN, a debilitating neurodegenerative disease that significantly reduces quality of life and for which there are currently no approved treatments in the United States. We recently completed a Phase 1/2 clinical trial studying AT-001 in approximately 120 patients with type 2 diabetes, in which no drug-related adverse effects or tolerability issues were observed. This trial also demonstrated target engagement and proof of biological activity, as measured by reduction in sorbitol, a biomarker of AR activity and NTproBNP, a marker of cardiac stress. In September 2019, we initiated a pivotal Phase 2/3 study in DbCM patients at high risk of progression to overt heart failure. The study also includes a DPN sub-study (in patients with both DbCM and DPN), which will inform our DPN development program.

We are also developing AT-003, an ARI designed to cross through the back of the eye when dosed orally, and has demonstrated strong retinal penetrance, for the treatment of diabetic retinopathy, or DR. DR is an ophthalmic disease that occurs in diabetic patients and for which treatments are currently limited to high-cost biologics requiring intravitreal administration. DR has been linked to AR activity, including elevations in sorbitol and subsequent changes in retinal blood vessels, which distorts vision and leads to permanent blindness. We are currently in late stages of preclinical development and intend to advance AT-003 into a Phase 1 clinical trial in 2020.

Our management team and scientific advisory board are composed of accomplished scientists and clinicians with decades of experience developing drugs for a wide range of diseases. Our view is that drug development does not always need to follow the standard approach, which often requires long and costly development programs before drugs become available to patients. By taking a unique and focused approach to drug development, we believe we can significantly shorten development programs and bring lifesaving drugs to patients in urgent need. In May 2019, we completed our initial public offering (the “IPO”) whereby we sold 4,000,000 shares of common stock at a public offering price of $10.00 per share, resulting in aggregate net proceeds of $34.6 million, after deducting underwriting discounts and commissions and offering expenses. In November 2019, we completed a private placement of 1,380,344 shares of our common stock (the “Private Placement”), which resulted in net proceeds of approximately $18.4 million. In January 2020, we completed a secondary public offering of 2,471,489 shares of our common stock, including 411,223 shares sold pursuant to the underwriters’ full exercise of their option to purchase additional shares (the “Secondary Public Offering”), pursuant to which we received $134.8 million of net proceeds, net of underwriting discounts and commissions and estimated offering expenses.

Our Strategy

Our goal is to bring potentially transformative therapies to market across a range of fatal or debilitating diseases for which no treatments are available. The critical components of our strategy include:

- ***Leveraging our unique approach to develop our pipeline of novel ARIs.*** We target molecules and pathways that have a proven role in disease, but have previously failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development utilizes recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on abbreviated regulatory pathways. We develop product candidates with increased potency and selectivity by leveraging recent technological advances in high throughput crystallography and in silico structural design. Our strategy is also informed by early use of biomarkers to confirm biological activity and target engagement. Early proof of biological activity through biomarkers in clinical trials combined with data from prior clinical development programs on first generation drugs significantly de-risks clinical development in our target indications. AR is our first molecular target that has been implicated in multiple diseases and for which sorbitol levels can be assessed as a biomarker of enzyme activity. Prior AR-targeting compounds produced nonselective inhibitors and failed to demonstrate adequate safety and efficacy. We intend to apply our strategy to a wide range of validated targets across multiple disease indications, which we believe will result in additional pipeline programs.

- ***Rapidly advancing the development of our ARI product candidates, AT-001, AT-007 and AT-003.*** We advanced AT-001 into a pivotal clinical trial in September 2019 for the treatment of DbCM. We plan to collect data on motor nerve conduction velocity, or MNCV, in this study in DbCM patients that also have DPN, which we expect will provide a basis for dose selection in Phase 3 clinical trials of DPN.

In June 2019, we initiated a pivotal Phase 1/2 study for AT-007 in healthy volunteers and adult galactosemia patients. The trial forms the basis of a future trial in pediatric patients to determine appropriate dosing in the pediatric population as well as the basis of a New Drug Application, or NDA, for treatment of galactosemia.

We intend to complete an investigational new drug application, or an IND, enabling program for AT-003 alongside animal efficacy models in DR to support a Phase 1 clinical trial in diabetic patients.

- ***Taking advantage of regulatory pathways designed for accelerated drug development in indications with high unmet need and seeking strategic partnerships in other indications.*** We plan to leverage abbreviated development programs and biomarker-based approaches for rapid drug development and regulatory approval. For indications that require standard development programs, we plan to seek strategic partnerships.

- ***Expanding our pipeline to products targeting other validated molecules and pathways outside of AR.*** We plan to further characterize our novel PI3K inhibitors and select lead compounds for preclinical development. Utilizing our biomarker-based approach, we intend to target urgent hematological oncology indications and specific solid tumors. We will continue leveraging our relationships with academic institutions and universities to acquire or license additional technologies that are consistent with our strategy of applying new technologies to validated molecular pathways.

Our Pipeline

The following table shows the status of our current ARI and PI3K inhibitor programs:

Compound	Preclinical	Phase 1	Phase 2	Phase 3	Dosing Route	Target Tissue	Milestones
Aldose Reductase Franchise							
AT-007	Galactosemia – Pivotal Ph 2 Study				Oral	CNS	Positive topline biomarker data reported Jan 2020
AT-001	Diabetic Cardiomyopathy – Pivotal Ph 3 Study				Oral	Systemic	Ph 3 trial initiated in Q3 2019; data in 2021
AT-001	Diabetic Peripheral Neuropathy				Oral	Peripheral Nerve	
AT-001	Acute Myocardial Infarction				SC*	Systemic / Peripheral Nerve	
AT-003	Diabetic Retinopathy				Oral	Retina	Preclinical data 2019; initiate Ph 1 2020
PI3 Kinase Franchise							
AT-104	PTCL, CTCL, TALL**				SC / Oral	Selective δ/γ inhibitor	Initiate Ph 1 2020

* Subcutaneous.

** Peripheral T-cell lymphoma, cutaneous T-cell lymphoma and T-cell acute lymphoblastic leukemia.

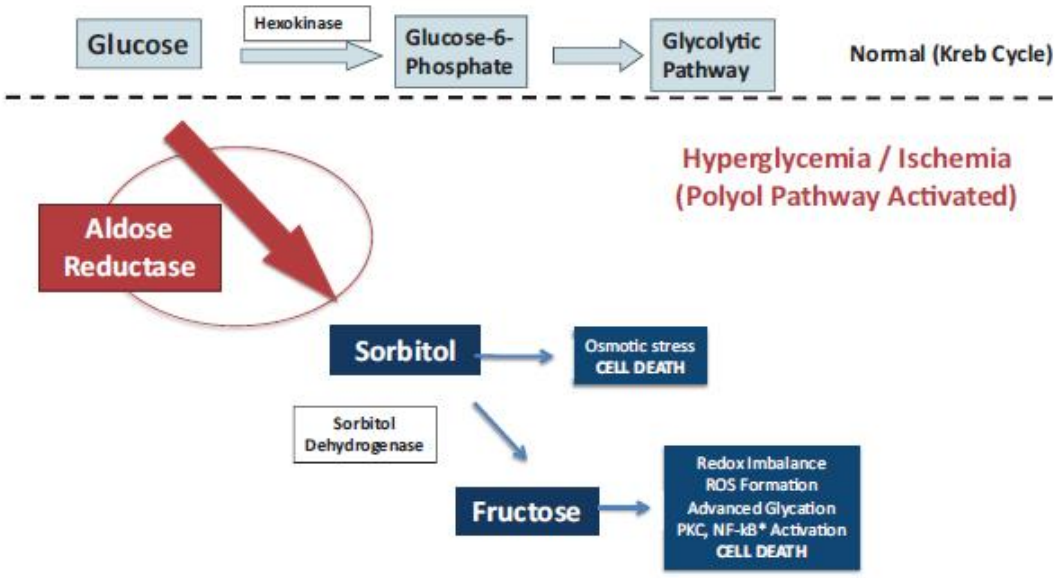
We seek to protect our proprietary and intellectual property position for our product candidates, our core technology, and other know-how through U.S. and foreign patent protection. To the extent that our platform is not patentable, we rely on trade secret protection and confidentiality agreements to protect our interests. For more information, see the section titled “Business — Intellectual Property.”

Our Product Candidates

Our Aldose Reductase Program

AR is the first enzyme and rate-limiting step in the polyol pathway, an alternative glucose metabolism pathway. AR is a redox-regulated enzyme that is activated by an altered redox state within the cell, which occurs during hyperglycemia and ischemia. AR activation is associated with downstream consequences of hyperglycemia, such as diabetic complications, as well as consequences of ischemia in the heart, such as acute myocardial infarction and chronic heart failure. As shown in the figure below, AR activity produces excess sorbitol, which causes osmotic dysregulation within cells and tissues, such as nerve and retina, and is toxic to many cell types, including cardiomyocytes. Sorbitol is also further metabolized to fructose, which initiates a cascade of metabolic dysregulation and inflammatory damage to cells, such as: reactive oxygen species, or ROS, generation; advanced glycation end products, or AGE; protein kinase C, or PKC, activation; and methylglyoxal overproduction. Under non-oxidative, or healthy patient conditions, AR remains largely inactive and less than 3% of a healthy person’s glucose is processed by the polyol pathway. However, when the oxidative environment of the cell changes due to hyperglycemia or ischemia, AR is both activated and upregulated, and greater than 30% of the patient’s glucose is then shunted through the polyol pathway, resulting in significant downstream damage to cells and tissues. The detrimental consequences of AR activation have been well established by decades of prior research. These include broad effects, such as mitochondrial dysfunction and cell death, as well as tissue-specific changes, such as neuronal degeneration in peripheral nerves, collagen crosslinking and fibrosis in cardiac tissue, and damage to blood vessels in the lens of the eye.

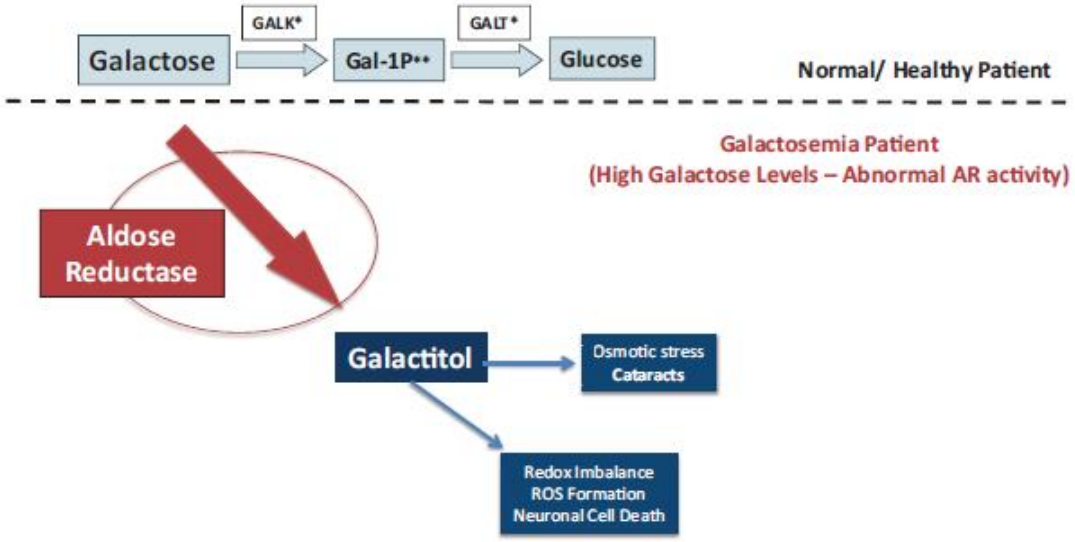
AR Causes Damage to Tissues Under Conditions of Oxidative Stress



* NF-kB is a protein complex that controls transcription of DNA, cytokine production and cell survival.

Additionally, as shown in the figure below, abnormal AR activity is associated with conversion of galactose to galactitol in patients with galactosemia. Galactitol, like sorbitol, does not cross the cell membrane and causes damage to cells across a wide range of tissues, including neurons in the brain, retinal cells in the eye and peripheral nerve tissue.

Galactitol Accumulation Results in Tissue Specific Damage



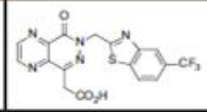
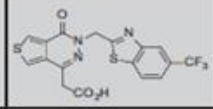
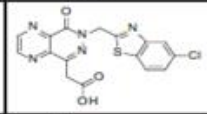
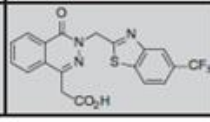
* GALK, or galactokinase, and GALT, or galactose-1-phosphate uridyl transferase, are enzymes that metabolize galactose.

** Galactose-1-phosphate is referred to as Gal-1P.

During the 1980s and 1990s, AR was a significant target of drug development due to its established role in a wide range of debilitating indications. Although these programs failed to produce effective drugs with a favorable risk/benefit profile, the prior ARI clinical development programs validated the role of AR in the pathogenesis of several diabetic complications and provided useful information on optimal patient criteria and trial design.

By applying new techniques in crystallography to better understand how the enzyme works, and applying in silico design and medicinal chemistry approaches, we have developed compounds with logarithmically improved potency and increased selectivity. Our technology includes specific compounds that are in various stages of preclinical and clinical development, and is coupled with an understanding of how the enzyme works and a knowledge base of structural approaches to drug the target while controlling drug characteristics, such as PK, solubility and tissue permeability.

The following table summarizes the current status of our AR program and compound differentiation:

Compound	Structure	IC_{50}[1]	Maximum Tolerated Dose in Animals	LogD[2]	Tissue Penetration (in rats)			
					Systemic/ Heart	Nerve	Retina	CNS
AT-001		30pM	>2,000 mg/kg	-1.00	✓	✓	✓	X
AT-007		100pM	>1,000 mg/kg	-0.09	✓	✓	✓	✓
AT-003		54pM	>1,000 mg/kg	-1.53	✓	✓	✓	X
Zopolrestat (prior Pfizer compound)		10nM	100 mg/kg	+0.06	✓	✓	X	X

(1) IC_{50} is the amount of a compound required to inhibit 50% of enzyme activity.

(2) LogD is a log of partition of a chemical compound between the lipid and aqueous phases. LogD often predicts retinal permeability, with compounds with negative LogD passing through the back of the eye.

AT-007 for the Treatment of Galactosemia

Overview

Our lead product candidate, AT-007, is a novel CNS penetrant ARI for the treatment of galactosemia, a devastating rare pediatric metabolic disease that affects how the body processes a simple sugar called galactose, and for

which there is no known cure or approved treatment available. High levels of galactose circulating in the blood and tissues of galactosemia patients enable AR to convert galactose to a toxic metabolite, galactitol, which results in long-term complications ranging from CNS dysfunction to cataracts. AT-007 was specifically designed to be a CNS penetrant to address AR activity in the brain and potentially prevent CNS consequences of the disease. We believe galactosemia qualifies for accelerated approval under recently released draft FDA guidance for low prevalence, slowly progressing rare metabolic diseases. The guidance allows for a biomarker-based development program if clinical efficacy and a link to a relevant biomarker can be demonstrated in an animal model of disease. We have demonstrated that treatment with AT-007 in an animal model of galactosemia reduces toxic galactitol levels and prevents disease complications. Additionally, we believe that pediatric galactosemia may qualify for the RPD-PRV program. In June 2019 we initiated a pivotal Phase 1/2 clinical study in healthy volunteers and adults with galactosemia examining safety, pharmacokinetics and biomarker effects of AT-007.

Diagnosis and Standard of Care

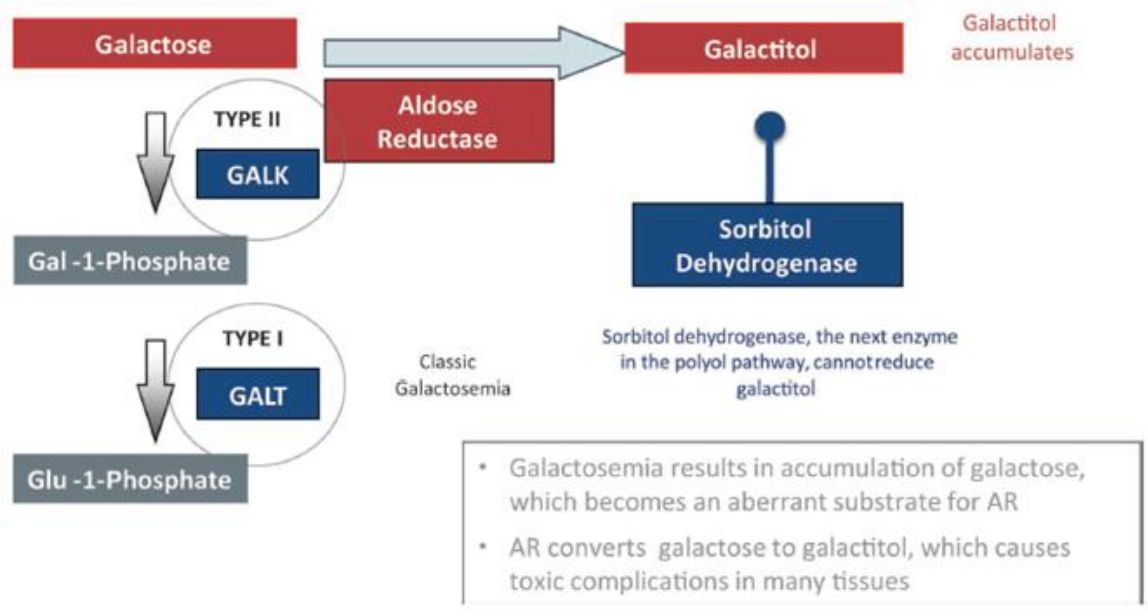
Galactosemia is caused by severe deficiency in the GALK or GALT enzymes that metabolize galactose. Galactose is a sugar produced endogenously by the body, and is also a metabolite of lactose. Galactosemia is often fatal in infants within the first weeks of life if they are exposed to dietary lactose in the form of breast milk or dairy-based formula. As such, there is mandatory newborn screening for galactosemia in the United States and many countries in Europe. While prompt identification of infants with galactosemia and immediate implementation of a lactose-restricted diet prevents many fatalities, long-term consequences of disease persist due to endogenous generation of galactose within the body. We are specifically developing AT-007 for patients with severe enzyme deficiencies in GALK, which is referred to as type 2 galactosemia, and GALT, which is referred to as classic galactosemia. In these patients, despite dietary restriction, galactosemia manifests as a combination of CNS and systemic toxicities in tissues, including cognitive dysfunction and intellectual deficiencies, speech and motor pathologies, pre-senile cataracts and tremor, as well as ovarian insufficiency in females.

Unlike severe forms of galactosemia, “clinical variant galactosemia” and “Duarte galactosemia” refer to partial reductions in various galactose metabolism enzymes; however, there does not appear to be any clinical consequence, as remaining activity is sufficient to metabolize galactose within the body. Patients with clinical variant and Duarte galactosemia do not require any intervention, in comparison to patients with severe GALK or GALT enzyme deficiencies.

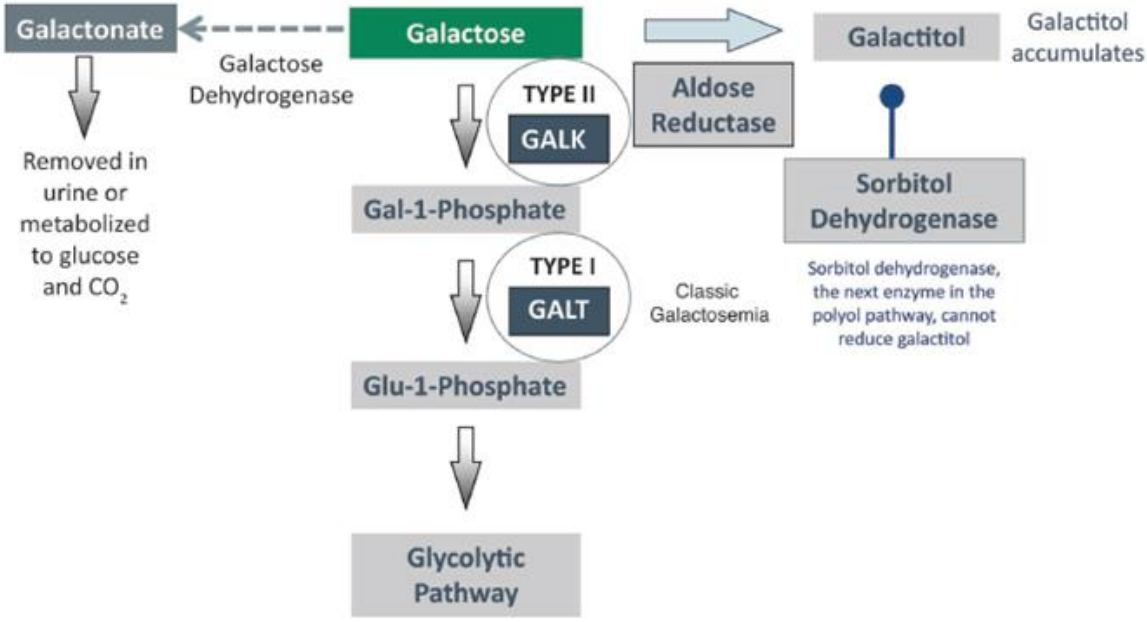
There are no treatments available for galactosemia, despite movement towards enzyme replacement therapy and gene editing and delivery technologies for many other rare diseases. This is because the major tissue-specific effects of galactosemia are seen in neurons in the brain, and delivery of recombinant enzymes, as well as gene delivery and editing, are difficult to accomplish across the blood-brain barrier and into neuronal cells, and current technologies have not yet been able to achieve therapeutic CNS delivery. Due to endogenous production of galactose within the body, infants with galactosemia develop significant complications even with immediate implementation of, and strict adherence to, a dairy-free diet. CNS complications include cognitive impairment, low IQ, speech and motor deficiencies, and infant or pediatric seizures. In addition, nearly all females develop ovarian insufficiency. Further to the damage that

occurs in childhood, many adults also develop persistent cataracts, tremor and seizures, due to ongoing tissue deposition of galactitol in the eyes and peripheral nerves.

AR Activity Causes Toxic Accumulation of Galactitol in Galactosemia



As shown in the figure below, we believe that blocking AR activity shifts galactose metabolism to an alternative enzyme called galactose dehydrogenase, which allows galactose to be metabolized to galactonate, a benign substance that is removed in the urine.



Market Opportunity

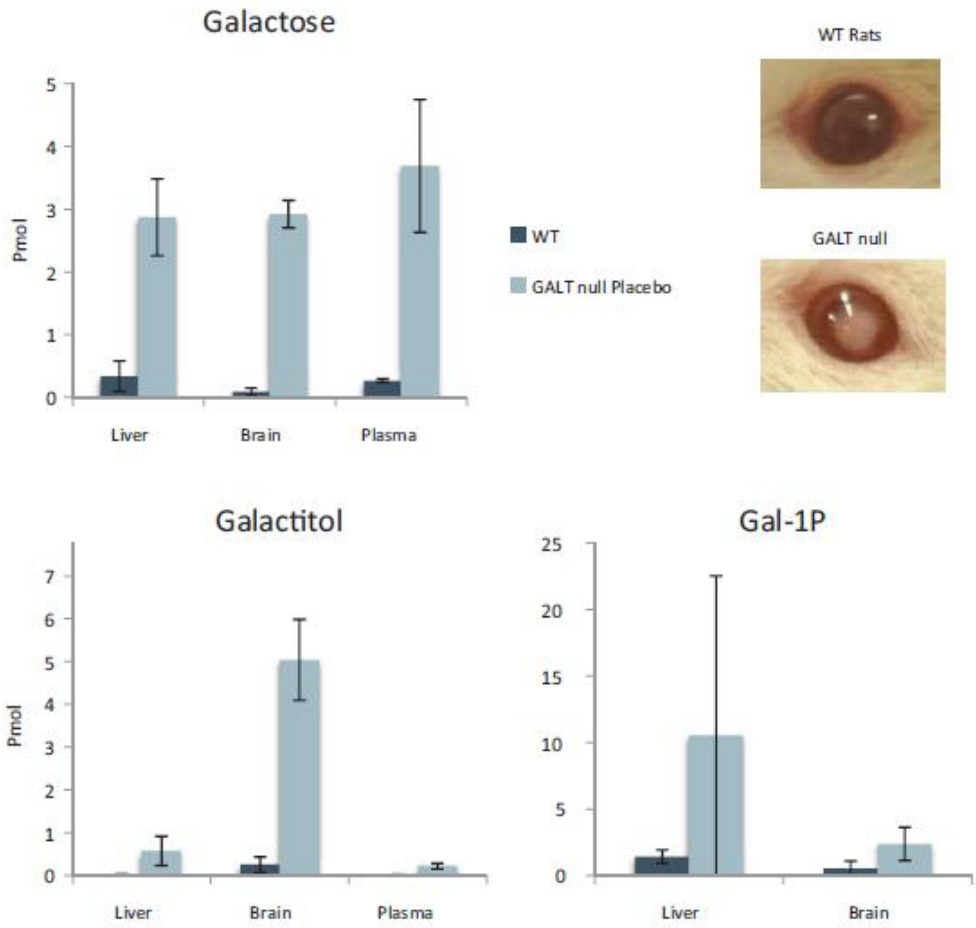
The global incidence of galactosemia is estimated to be 1 in 50,000 to 1 in 90,000, depending on ethnicity. However, we believe that the U.S. galactosemia population is approximately 2,800 patients, based on newborn screening data identifying 2,500 infants through 2014, and the estimated birth rate of 80 patients per year. Prior studies estimated that the U.S. galactosemia population was higher based on the incidence rates, because they did not take into account that, prior to newborn screening, most infants with galactosemia died within a few weeks of birth. As a result, the disease prevalence is significantly lower, and the live population with galactosemia is largely age 40 and younger.

Preclinical Studies

A rat model of classic galactosemia, or GALT null, was recently developed at Emory University, and was shown to display similar levels of galactose and metabolites in blood and tissues to that of galactosemia patients. These rats develop many of the long-term complications associated with galactosemia in humans, including bilateral cataracts, as well as CNS deficiencies in motor coordination, cognition and learning, as quantified by rotarod and water maze

testing. Characteristics of this model, including cataracts and high levels of galactose, galactitol and Gal-1P in blood and tissues such as liver and brain, are shown in the figure below.

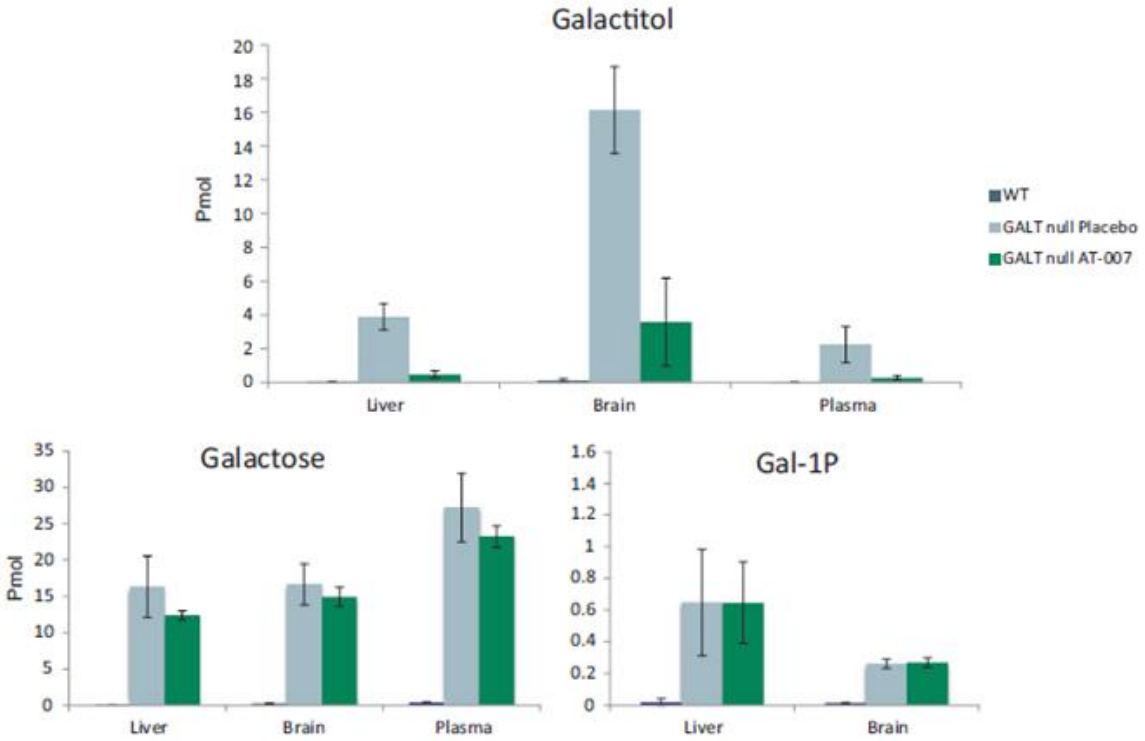
Animal Model of GALT Deficiency



As shown in the figures below, treatment with AT-007 in neonatal GALT null rats from day 1 to day 10 significantly reduced galactitol levels in target tissues, including blood, brain and liver, without increasing galactose or Gal-1P levels, and prevented complications associated with galactitol accumulation in tissues, including cataract formation and CNS dysfunction. The effects of AT-007 were dose dependent and corresponded with galactitol reduction.

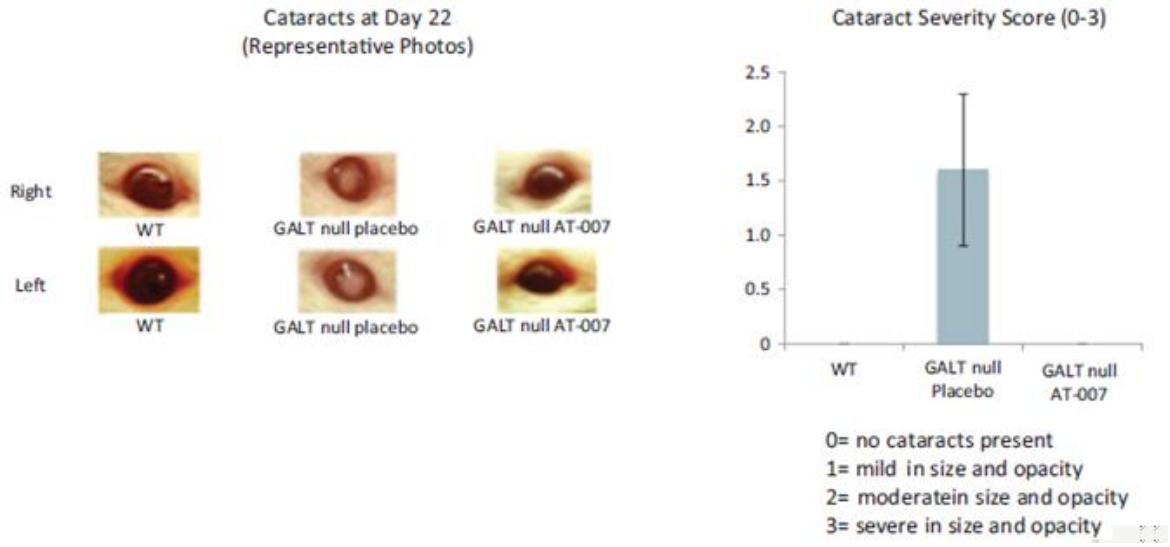
Rats treated with AT-007 also displayed reduced galactonate levels, supporting our hypothesis that ARIs increase metabolism of galactose by galactonate dehydrogenase.

AT-007 Treatment Significantly Reduced Galactitol Levels in Liver, Brain and Plasma



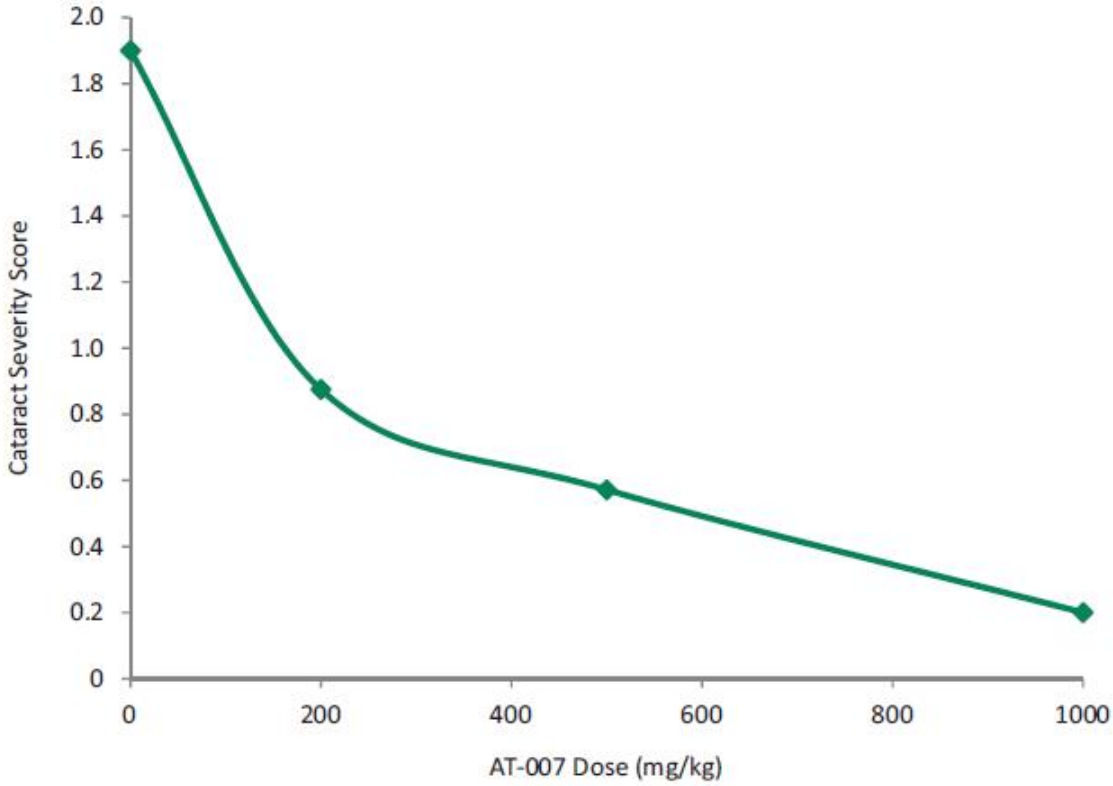
Similar reductions in galactitol were observed at day 22 and at five months. Additionally, AT-007 prevented cataract formation in newborn rats at day 10, day 22 (as shown in the figure below) and at five months.

AT-007 Treatment Prevented Cataract Formation in Newborn Rats

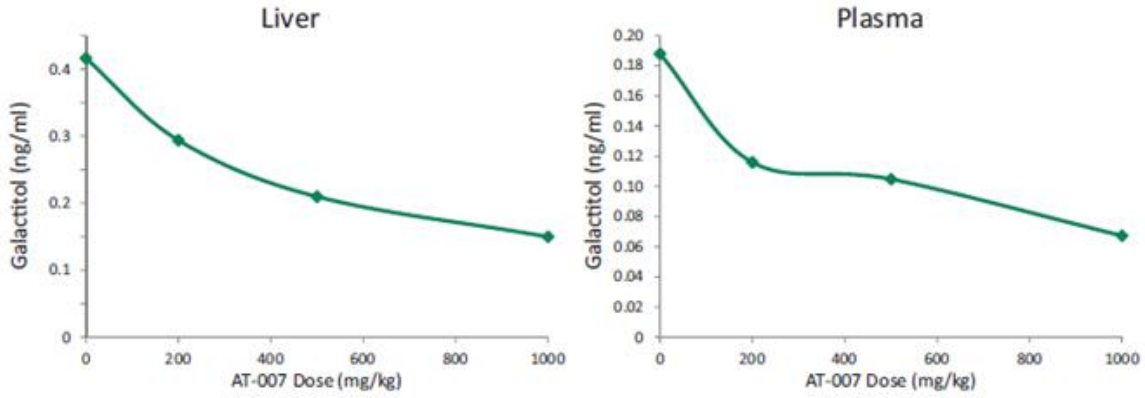


As shown in the figures below, greater doses of AT-007 reduced galactitol levels and the severity of cataracts.

AT-007 Cataract Dose Response

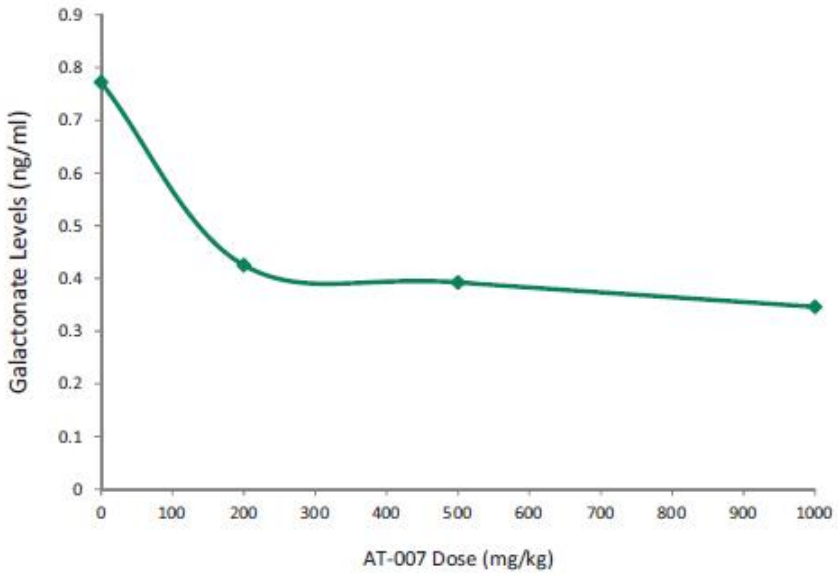


AT-007 Galactitol Reduction Dose Response



As shown in the figure below, AT-007 reduced galactonate levels, which we believe supports our hypothesis that AR inhibition activates galactonate dehydrogenase.

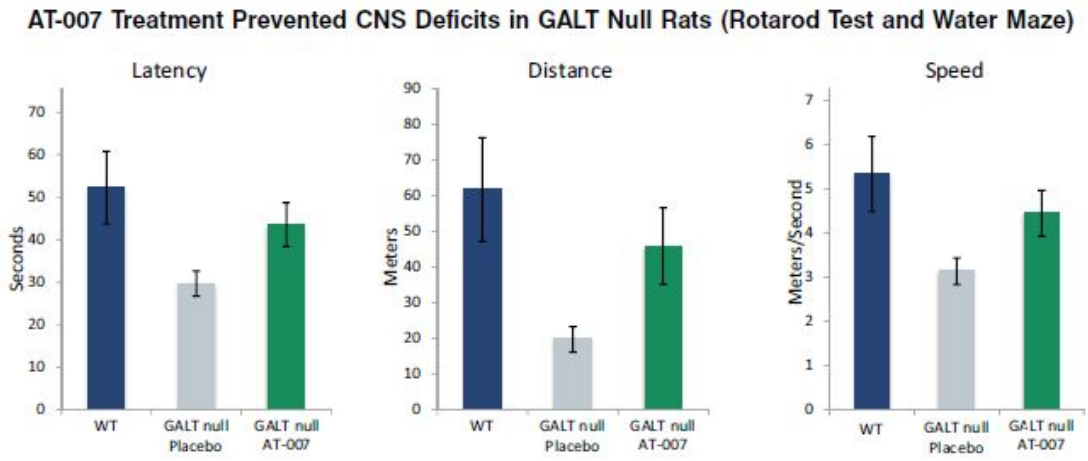
AT-007 Reduced Galactonate Levels at Day 22



WT and GALT null rats were treated daily with AT-007 for five months, beginning on the day after birth, and were tested for cognitive outcomes via rotarod and water maze testing. Generally, rotarod tests both learning and motor coordination, while water maze tests intelligence and cognitive ability.

As shown in the figure below, while galactosemic rats show deficits in learning and motor coordination versus WT rats, treatment with AT-007 was able to prevent these deficiencies and normalize cognitive and motor function as measured by both rotarod and water maze testing.

AT-007 Treatment Prevented CNS Deficits in GALT Null Rats (Rotarod Test)



Clinical Development Plan

We have evaluated AT-007 in a pivotal Phase 1/2 clinical trial in healthy volunteers and adults with galactosemia. Although much of the CNS damage seen in adults is permanent and irreversible, prevention of further damage to tissues that occurs throughout adult life, such as cataract formation, seizures and tremor, may provide significant quality of life benefits to galactosemic adults. In pediatric studies we will seek to prevent any tissue damage from occurring, including neuronal damage in the brain that results in cognitive, intellectual, speech and motor deficits in infants and children.

The Phase 1 clinical trial was split into two parts — Phase 1 in healthy volunteers and Phase 2 in adults with galactosemia. The Phase 1 portion in healthy volunteers is designed as a SAD and MAD clinical trial in 24 to 32 healthy volunteers, six to eight patients per cohort, with two patients receiving placebo. The Phase 1 evaluated safety, tolerability and PK of AT-007 at doses of 5mg/kg to 20mg/kg per day via once daily dosing. The MAD portion of the trial studied seven days of consecutive treatment at 5-20mg/kg per day. The Phase 2 portion in adults with galactosemia was designed as an adaptive trial in 12 to 18 patients, with up to six patients per cohort. The Phase 2 portion evaluated safety, tolerability and PK in adult patients with galactosemia. Patients received either AT-007 5mg/kg, AT-007 20mg/kg or placebo, receiving a single dose four days prior to receiving 27 days of consecutive dosing. Biomarker levels of galactose and galactose metabolites, including galactitol, were also measured in these patients to determine target engagement and proof of biological activity.

On January 8, 2020, we announced positive topline results from the pivotal Phase 2 portion of the ACTION-Galactosemia study of AT-007, a CNS penetrant AR inhibitor, in adult galactosemia patients. ACTION-Galactosemia is a double-blind placebo-controlled trial evaluating safety and pharmacokinetics of AT-007 in healthy volunteers, as well as safety, pharmacokinetics and biomarker effects in adult galactosemia patients over 28 days of once daily oral dosing. The key biomarker outcome of the study was reduction in galactitol, an aberrant toxic metabolite of galactose, formed by AR in galactosemia patients.

AT-007 treatment resulted in a statistically significant and robust reduction in plasma galactitol versus placebo in adult galactosemia patients. Reductions in galactitol were dose dependent, with higher concentrations of AT-007

resulting in a greater magnitude of reduction in galactitol. At the highest dose tested (20mg/kg), AT-007 significantly reduced plasma galactitol 45-54% from baseline versus placebo (with a p value of less than 0.01). Galactitol reduction was rapid and sustained over time. No substantial change from baseline was observed in placebo treated patients. AT-007 was well tolerated, with no drug-related adverse events noted to date in galactosemia patients or in the 72 healthy volunteers treated in Part 1 of the trial.

We plan to utilize recent FDA guidance permitting biomarker-based development in low prevalence, slowly progressing rare metabolic diseases, such as galactosemia, and expects to file for regulatory approval in the second half of 2020.

Due to the early role of endogenous galactose production and resulting galactitol levels on neuronal damage, there is an urgency to treat prior to damage occurring. We plan to move as quickly as possible in clinical development from adults to children. We believe that a pediatric indication in galactosemia may qualify for the RPD-PRV program.

AT-001 for the Treatment of Diabetic Cardiomyopathy

Overview

We are developing AT-001, a novel ARI with broad systemic exposure and peripheral nerve permeability being developed for the treatment of DbCM, a fatal fibrosis of the heart, for which no treatments are available. We recently completed a Phase 1/2 clinical trial evaluating AT-001 in approximately 120 patients with type 2 diabetes, in which no drug-related adverse effects or tolerability issues were observed. This trial also demonstrated target engagement and proof of biological activity, as measured by reduction in sorbitol, a biomarker of AR activity and NTproBNP. In September 2019, we initiated a pivotal Phase 2/3 study in DbCM patients at high risk of progression to overt heart failure.

Diagnosis and Standard of Care

DbCM is a fatal fibrosis of the heart that occurs in both type 1 and type 2 diabetic patients, which leads to decreased contractility and decreased heart function, eventually resulting in fulminant heart failure. DbCM is caused by metabolic derangements in cardiomyocytes that result in cell death and fibrosis. AR activity has been shown to be a large contributor to these metabolic derangements, and the downstream effect of AR activation is responsible for the cardiomyocyte cell death and fibrosis. DbCM is diagnosed by increased weight of the heart and decreased contractility, which are identified by echocardiographic screening, as well as by exclusion of other forms of heart disease. Epidemiological studies have shown that approximately 17% to 24% of diabetic patients display DbCM in the absence of any other forms of heart disease. These patients do not have hypertension, atherosclerosis, valvular heart disease or ischemia, and the only cause of the cardiomyopathy is the underlying diabetes. Stages of DbCM range from asymptomatic, or stage 1, to acute heart failure, or stage 4. Most patients are not diagnosed until stage 2, where heart function approaches 50% of normal and symptoms manifest as extreme shortness of breath during exercise, referred to as decreased exercise tolerance. Exercise tolerance in these patients (as measured by maximum amount of oxygen a person can utilize during intense exercise known as peak VO2) is approximately 25% lower than diabetic patients without DbCM, and decreases by an additional 30% as the patients progress to overt heart failure in later stages of diseases. Patients quickly progress at a steady state of decline to stage 3, which includes marked cavity dilation and severe limitations in daily activities. The final stage of DbCM, stage 4, is represented by acute heart failure resulting in death. The current standard of care is to target glucose control in these patients, as well as hemodynamic modulation of blood flow, through use of beta blockers and diuretics. Both approaches are largely ineffective, and DbCM often results in death within five to ten years of diagnosis. Approximately 24% of DbCM patients progress to overt heart failure or death within 1.5 years of diagnosis, and 37% within five years of diagnosis.

Market Opportunity

According to a retrospective epidemiological study, approximately 17% of patients suffering from diabetes develop DbCM. A more recent study completed in France that utilized echocardiographic screening estimates the proportion of diabetic patients to develop DbCM at approximately 24%. The International Diabetes Foundation estimated that there were approximately 451 million patients globally with diabetes in 2017, which is expected to

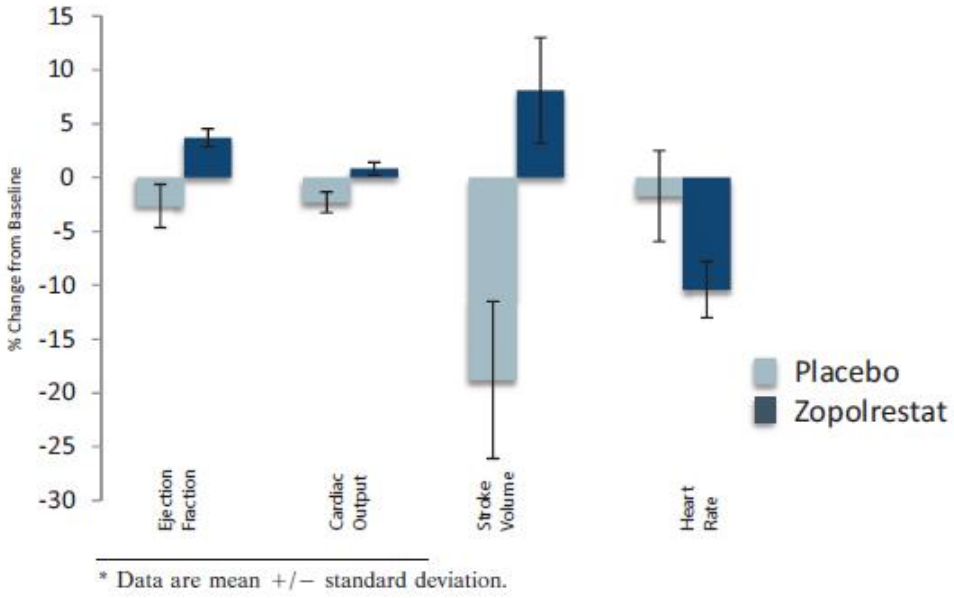
increase to 693 million by 2045. This includes 58.0 million diabetes patients in Europe in 2017, which is expected to increase to 67.0 million in 2045, and 46.0 million in North America, which is expected to increase to 62.0 million in 2045. Based on an estimated prevalence of 17% of diabetic patients who develop DbCM, we estimate that currently there are approximately 77.0 million patients with DbCM globally, with approximately 8.0 million in North America and 10.0 million in Europe. Initially, our development program will target stage 2 and 3 patients, which we estimate constitute approximately 50% of all DbCM patients. We believe these patients represent a symptomatic population that is more likely to be responsive to treatment. Stage 1 and 4 patients represent an additional market opportunity, which we plan to explore in a post-approval setting.

Prior AR-Based Approaches to Treat DbCM

AR activity has been implicated as a strong contributing factor to pathogenesis in DbCM. Pfizer Inc. was developing an ARI, Alond (zopolrestat), for the treatment of DPN and DbCM in a Phase 2 clinical trial that demonstrated favorable outcomes on heart function in DbCM patients, but the clinical trial was discontinued due to an unfavorable risk/benefit profile, with several patients experiencing liver toxicity and significant elevations in both aspartate aminotransferase and alanine aminotransferase, which are enzymes central to identification of liver toxicity and damage. In this trial, patients with early-stage DbCM were identified by echocardiographic screening and were randomized to three treatment groups, which consisted of placebo, 500 mg zopolrestat per day or 1,000 mg zopolrestat per day dosed for one year. Due to liver toxicity seen in another trial with zopolrestat, the 1,000 mg treatment arm was reduced to 500 mg, and the two doses were collapsed into one treatment arm. While patients on placebo displayed decreased heart function over the year of the trial as their disease progressed, patients on zopolrestat displayed a stabilization of heart function and even improvement in heart function in some patients based on hemodynamic endpoints. As shown in the figure below, after one year of ARI treatment, there were statistically significant increases in resting left ventricular ejection fraction, or LVEF ($p<0.02$), cardiac output ($p<0.03$), left ventricular, or LV, stroke volume ($p<0.004$), and exercise LVEF ($p<0.001$). In placebo-treated subjects, there were statistically significant decreases in exercise LVEF, cardiac output and stroke volume. Exercise LVEF increased with ARI treatment independent of blood pressure, insulin use or the presence of baseline abnormal heart rate variability. There was no change in resting diastolic filling rates in either group. This trial demonstrated that abnormalities in systolic function in patients with DbCM can be stabilized and partially reversed by ARI treatment. We believe this data validates the

approach of using an ARI to improve outcomes for patients with DbCM and using our compounds, which demonstrate improved potency and have been well tolerated, may lead to greater clinical utility.

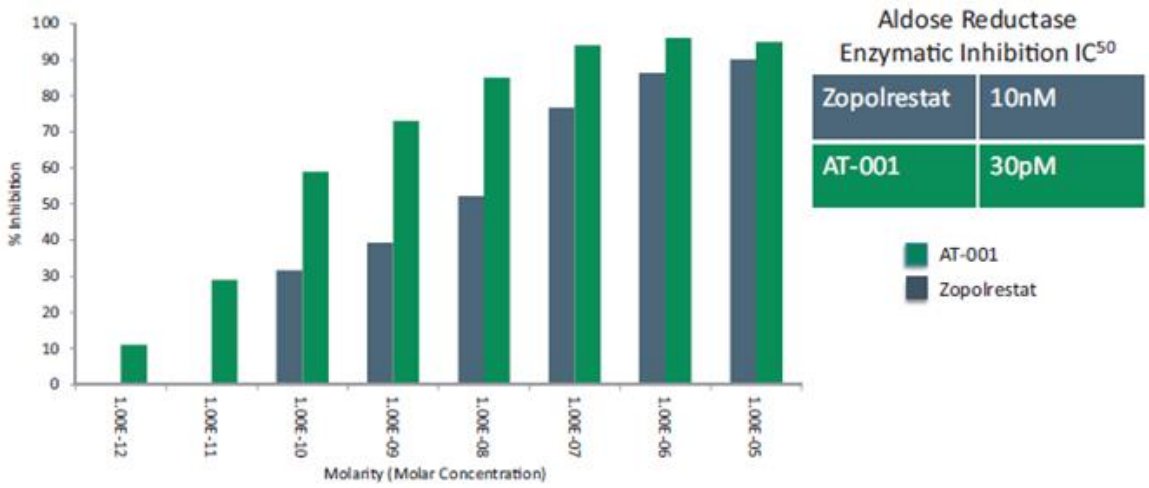
Cardiac Function at 12 Months on Maximal Exercise



* Data are mean +/− standard deviation.

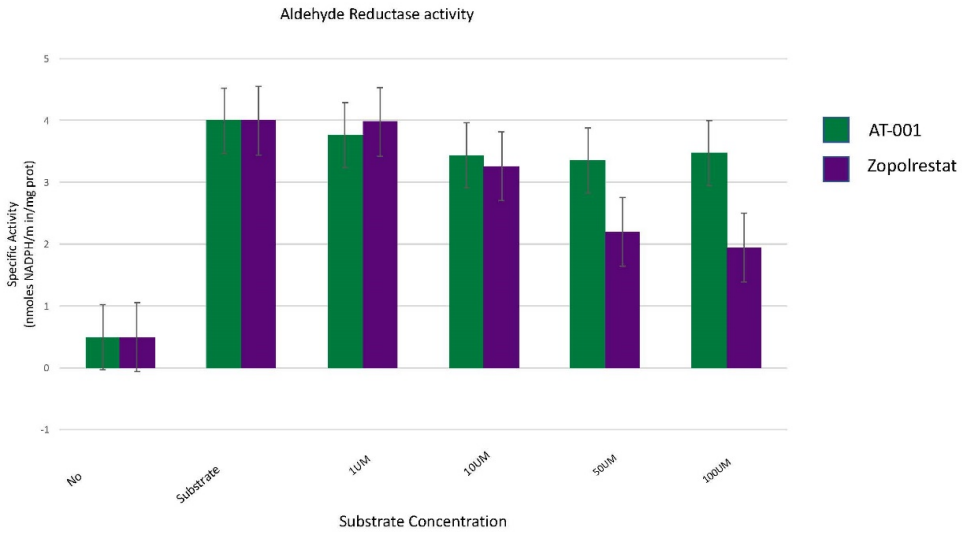
As shown in the figure below, when compared to zopolrestat, AT-001 has significantly higher in vitro enzymatic inhibitory activity. IC50 and IC90, or the amount of a compound required to inhibit 90% enzyme activity, are typically calculated by determining the level of enzymatic inhibition at ten-fold dilutions, moving to smaller concentrations of the inhibitory compound. At lower concentrations of compound, AT-001 demonstrated logarithmically greater enzymatic inhibition versus zopolrestat. Similarly, the IC50 of AT-001 was determined to be 30pM, nearly 1,000 fold lower than that of zopolrestat, which is 10nM. Zopolrestat demonstrated liver toxicity as a side effect in several clinical studies, which was believed to be due not to AR inhibition, but due to off-target inhibition of a structurally related enzyme, Aldehyde Reductase, which is required for normal liver function. AT-001 demonstrates increased selectivity for AR, and does not inhibit Aldehyde Reductase at any concentration tested. This increased selectivity led to lack of toxicity in cultured hepatocytes, or liver cells, whereas zopolrestat demonstrated significant toxicity in hepatocytes as shown in the figures below. Thus, we believe that not only is AT-001 a more potent AR inhibitor than prior drugs, but that we have overcome the safety and toxicity limitations from prior compounds, which were due to lack of selectivity and off-target inhibition of Aldehyde Reductase.

***In vitro* Aldose Reductase Activity AT-001 versus Zopolrestat**

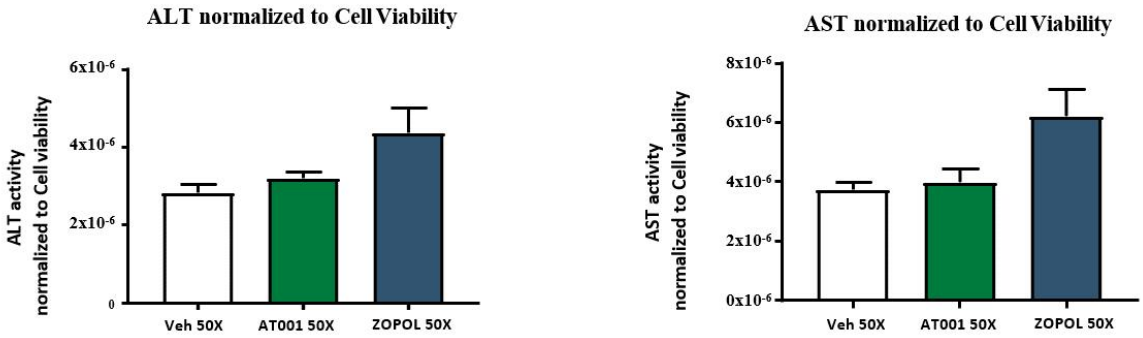


In Vitro Aldehyde Reductase Activity AT-001 vs. Zopolrestat

Aldehyde Reductase Activity



Hepatotoxicity in Cultured Liver Cells AT-001 vs. Zopolrestat



Recently Completed and Ongoing Clinical Trials

We have recently evaluated AT-001 in a placebo-controlled Phase 1/2 single ascending dose, or SAD, and multiple ascending dose, or MAD, clinical trial in approximately 120 type 2 diabetes patients. The primary objectives of this trial were to explore the safety, tolerability and PK profile of AT-001. Because AR converts glucose to sorbitol, and AR activity is elevated in diabetic patients, sorbitol normalization was also examined as a pharmacodynamic, or PD, biomarker of target engagement, which provided proof of biological activity in patients.

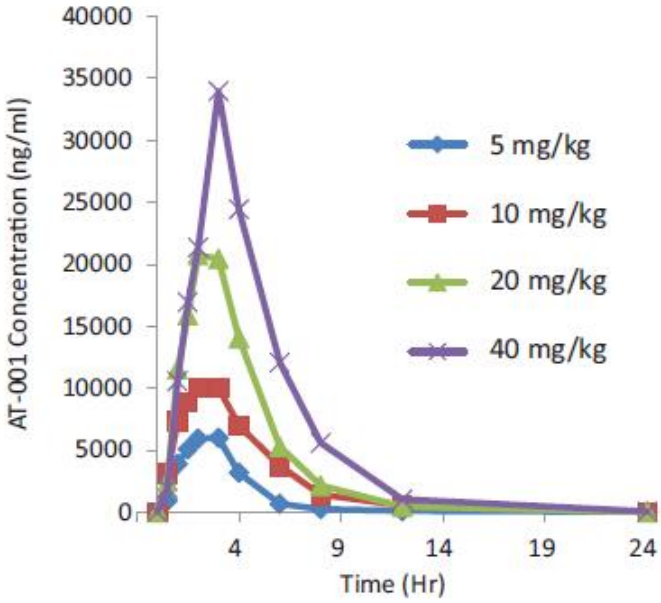
The Phase 1/2 clinical trial allowed use of concomitant treatments for glucose control, as well as other standard of care treatments for diabetes, such as statins and ACE inhibitors. The FDA permitted us to directly evaluate diabetic patients due to positive data from the preclinical studies, as well as the urgency to develop drugs quickly due to high unmet need. AT-001 was dosed as an active pharmaceutical ingredient, or API, powder in a rapid release capsule and the trial examined both once-daily and twice-daily, or BID, dosing regimens. We have completed the initial safety, pharmacology and biomarker studies up to seven consecutive days of treatment. No drug-related adverse effects or tolerability issues were observed at any single or multiple doses of AT-001. Treatment with AT-001 did not cause any abnormalities in vital signs or electrocardiogram, and did not cause an increase in glucose levels. Additionally, there were no observed adverse interactions with any concomitant diabetes medications used by patients during the trial.

SAD Portion of the Trial

Our SAD trial was conducted on 40 type 2 diabetes patients, ten patients per cohort, with eight patients receiving AT-001 and two patients receiving placebo. The patients were dosed under fasted conditions and received breakfast two hours post dose. Hourly blood samples were taken for PK and sorbitol measurements over a 12-hour period and again at 24 hours. Our initial dose of 5 mg/kg dosed orally was observed to have an effect on sorbitol levels in patients. Although we observed an effect on AR activity at the lowest dose of 5 mg/kg, we continued to dose escalate up to 40 mg/kg. Unlike prior compounds that were often limited by tolerability and safety issues, our compound did not demonstrate safety or tolerability limitations up to the maximum tested dose of 40 mg/kg. As shown in the figure below,

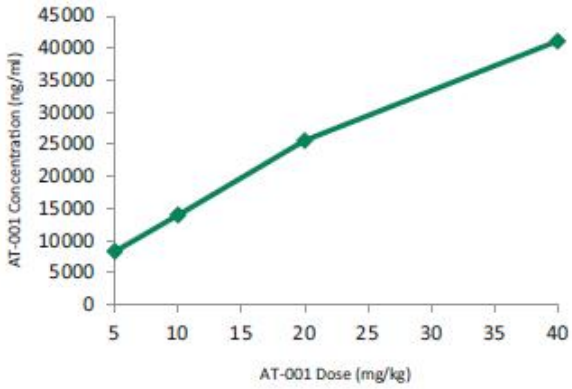
dose-response impact from 5 mg/kg to 40 mg/kg was observed on PK endpoints, providing adequate information for future dose selection.

PK Timeframe for AT-001 Phase 1/2 SAD Cohorts
(each curve represents the mean of eight patients)

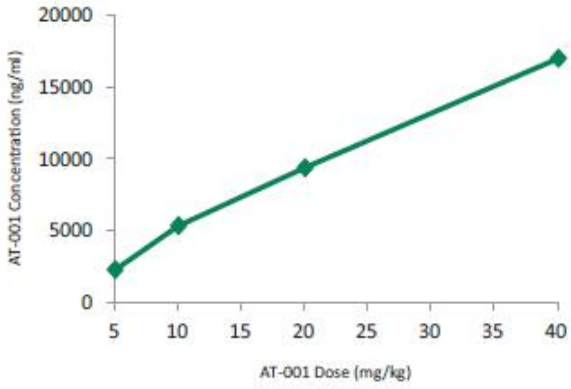


As shown in the figures below, AT-001 demonstrated a linear PK profile, which we believe evidences a predictable dose response.

AT-001 Maximum Concentration (C_{max}[(1)] mean)



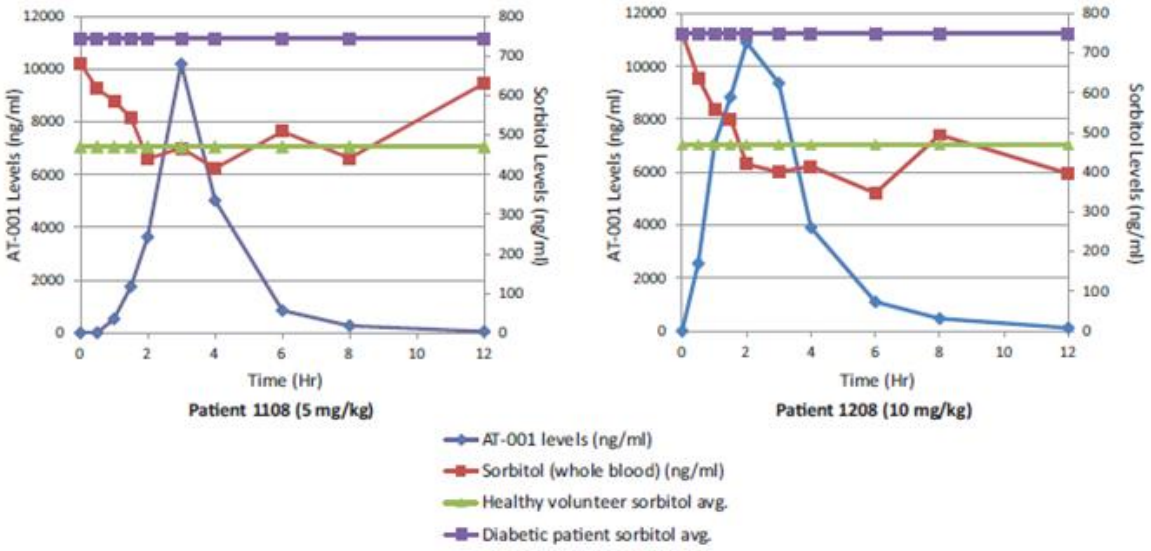
AT-001 Area Under the Curve (AUC mean)



(1) C_{max} is the highest concentration of a drug in the blood after a dose is given.

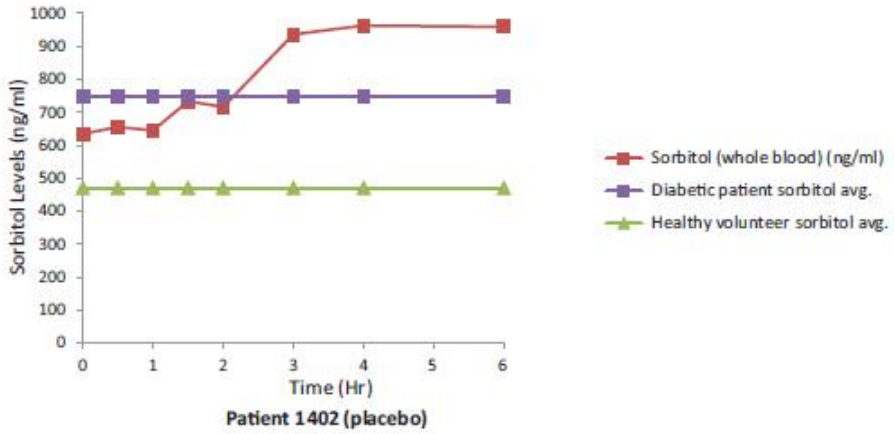
Because AR converts glucose to sorbitol, and AR activity is elevated in diabetic patients, sorbitol normalization to healthy subject levels can be used as a PD biomarker of target engagement and proof of biological activity. As shown in the figures below, which is representative of the AT-001-treated patients in the trial, as levels of AT-001 increase in the patients' blood, sorbitol levels are significantly reduced.

Representative PK Curves of AT-001 and Whole Blood Sorbitol Levels in Patients Treated with AT-001



As shown in the figure below, which is representative of the placebo-treated patients in the trial, this effect was not observed in placebo patients, who demonstrated sorbitol increases over the timeframe of drug-related sorbitol reduction, due to food effects on sorbitol. These patients were given breakfast two hours post dose.

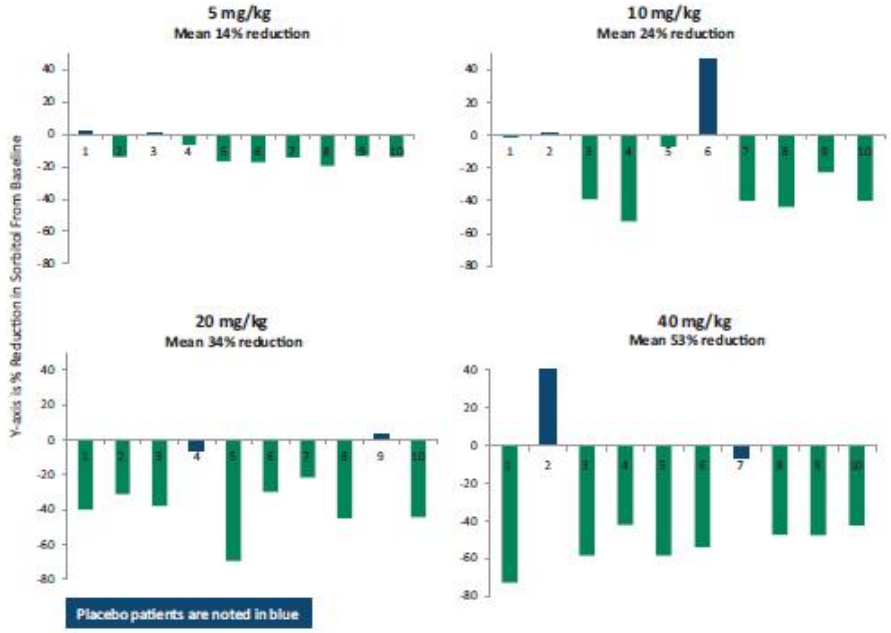
Representative Curve of Whole Blood Sorbitol Levels in Placebo-Treated Patients



As shown in the figure below, a dose response was observed when percent reduction in sorbitol levels was calculated at the C_{max} of the drug, which is approximately two hours, demonstrating higher reductions in sorbitol at

higher doses of AT-001. Average sorbitol levels of healthy volunteers were observed to be approximately 470 ng/ml and approximately 750 ng/ml for diabetic patients. The average net difference in sorbitol levels between diabetic patients and healthy volunteers represents the approximate amount of sorbitol generated by abnormal AR activity, which is approximately 50% reduction on average. Baseline sorbitol levels seen in healthy volunteers are believed to be primarily due to dietary intake of sorbitol, as well as baseline AR activity, which is approximately 3% glucose metabolism through AR in healthy volunteers.

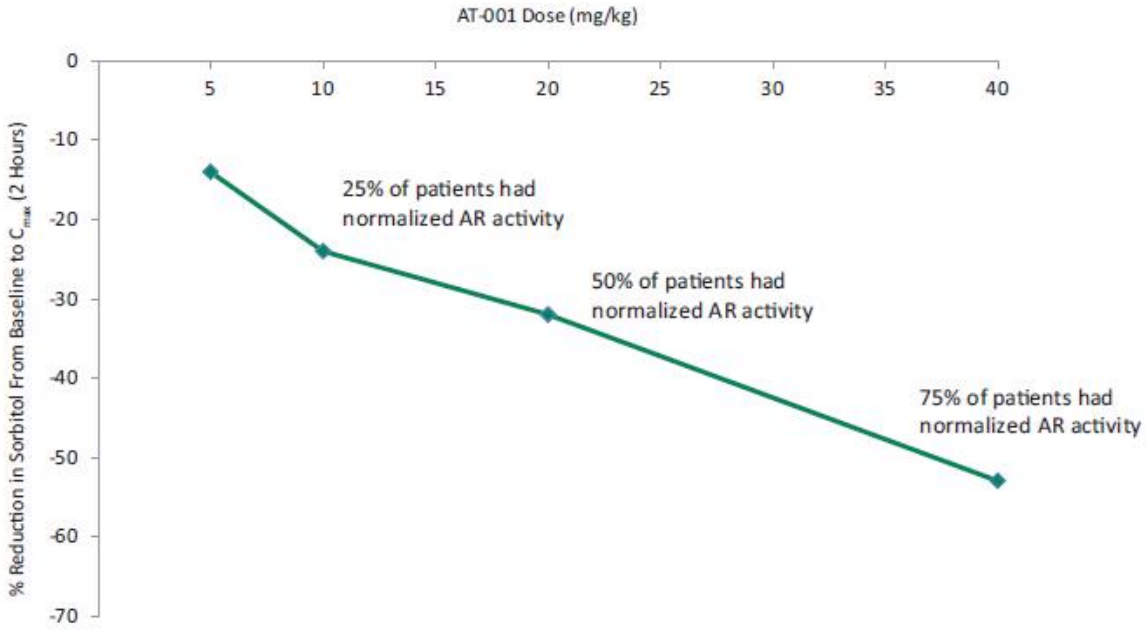
AT-001 Percent Reduction in Sorbitol, SAD Cohorts A1-A4



The figure below depicts the average reduction in sorbitol from baseline to Cmax of two hours from each dose cohort, as captured by the figure above. Based on our trials, we believe the complete inhibition of aberrant AR activity seen in diabetic patients corresponds to an approximately 50% reduction in elevated sorbitol levels to the healthy

volunteer average of 470 ng/ml. This was achieved in 25% of patients dosed at 10 mg/kg, 50% of patients dosed at 20 mg/kg and 75% of patients dosed at 40 mg/kg.

AT-001 Mean Reduction in Sorbitol by Dose, SAD Cohorts A1-A4

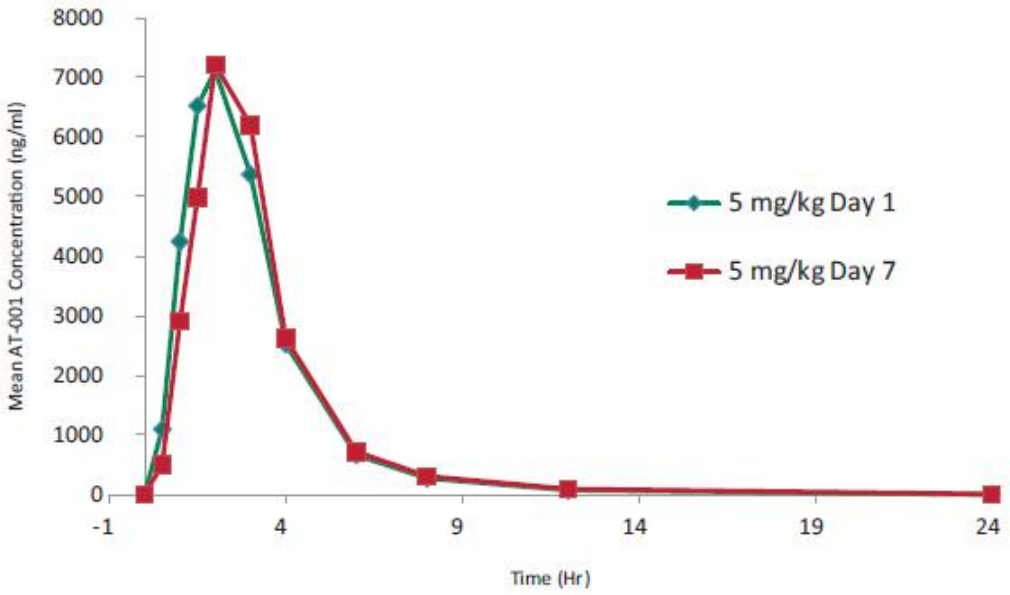


MAD Portion of the Trial

Our MAD trial was conducted on 40 type 2 diabetes patients, ten patients per cohort, with eight patients receiving AT-001 and two patients receiving placebo. The patients were dosed for seven consecutive days with 5 mg/kg, 20 mg/kg and 40 mg/kg once daily, or 20 mg/kg twice daily. Hourly blood samples were taken for PK and sorbitol measurements over a 12-hour period and again at 24 hours on days one and seven.

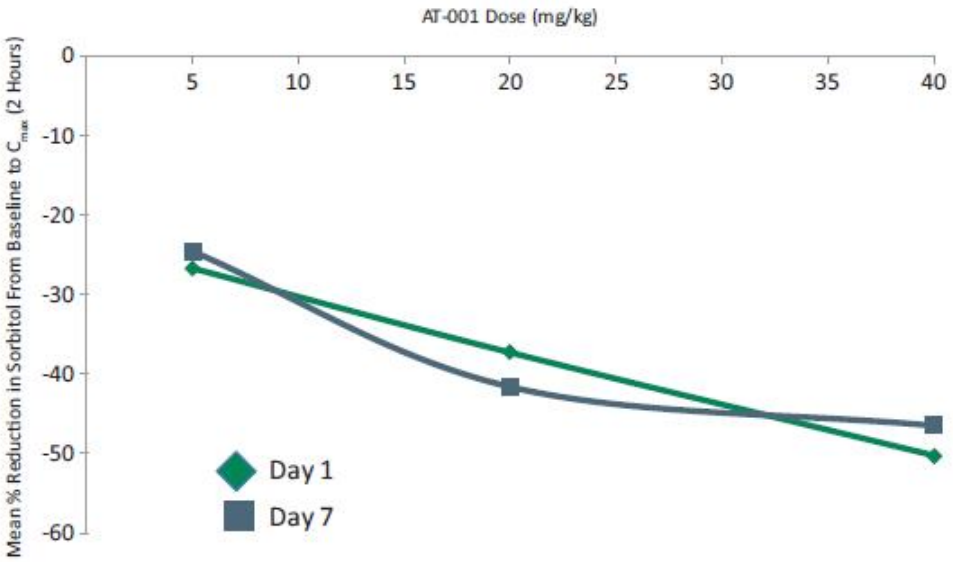
As shown in the figure below, PK profile of AT-001 was similar on days one and seven, suggesting there was no first pass clearance or other PK effects due to repeat dosing over this time period.

AT-001 Multiple Dose PK Profile—No First Pass Clearance or Drug Accumulation at 5 mg/kg



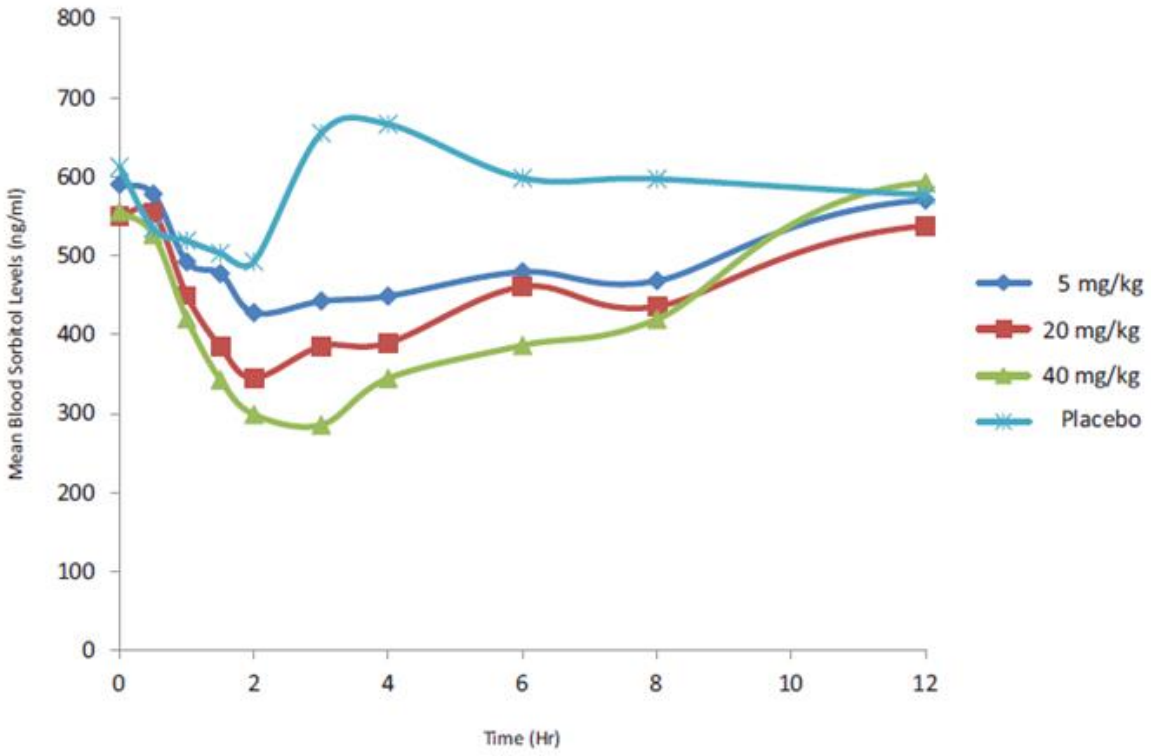
As shown in the figure below, effects on sorbitol from baseline to Cmax of two hours from each dose cohort were similar at day one and day seven, indicating that there is no correction for AT-001 effects in diabetic patients over this time period.

Comparison of % Reduction in Sorbitol from Baseline to C_{max} at Day 1 and Day 7 of Dosing



The figure below shows the effect on sorbitol levels over a 12-hour period in patients treated with 5 mg/kg, 20 mg/kg and 40 mg/kg doses versus placebo. Treatment with AT-001 resulted in dose-dependent AR inhibition as measured by sorbitol reduction over a 10- to 12-hour period.

Effect of AT-001 on Sorbitol Levels Over 12 Hours



Protection from Post-Prandial AR Activation in Diabetic Patients

The diabetic patients enrolled in this trial had well-controlled blood glucose levels. However, these patients still experienced periods of transient worsening of hyperglycemia, specifically following meals when there is excess glucose available. This transient post-prandial response leads to further activation of AR and is seen as an increase in blood sorbitol levels following meals in placebo treated patients, as shown in the figure above and in prior figures. Patients receiving AT-001 not only demonstrated reduced sorbitol levels, but were also protected from post-prandial AR activation.

Phase 2a in DbCM Patients

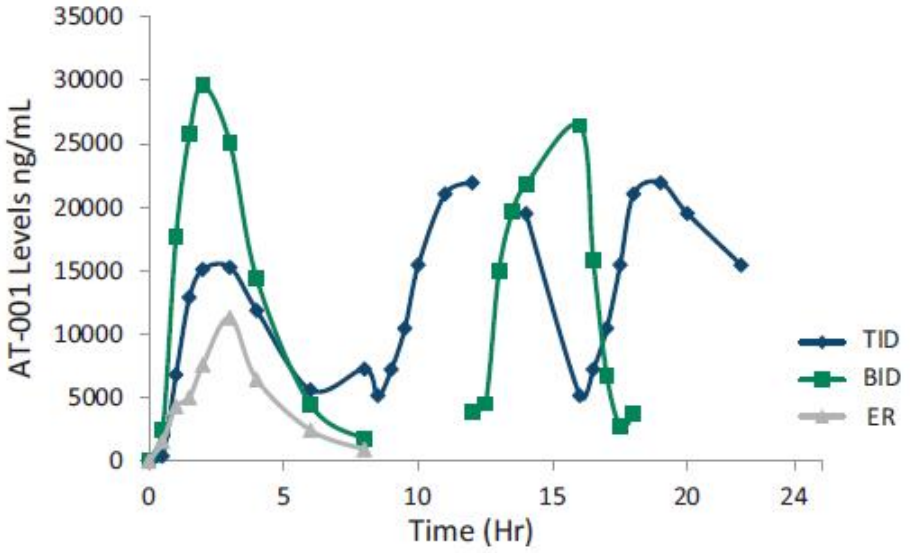
We have completed an extension to our Phase 1/2 clinical trial to evaluate the safety, tolerability and PK of AT-001 over a 28-day treatment period in approximately 30 type 2 diabetes patients with early-stage DbCM. The primary objectives were to explore the safety and tolerability of AT-001 over 28 days in patients with early-stage DbCM, and to examine the PK profiles of a flat dose of 3,000 mg per patient administered via three different dosing formulations and posologies: (1) a once-daily extended release, or ER, formulation in the form of four 750 mg tablets, (2) 1,500 mg BID rapid release capsule 12 hours apart and (3) 1,000 mg three times daily, or TID, eight hours apart. Additionally, many DbCM patients displayed elevated levels of a cardiac biomarker, NTproBNP, which can be

examined alongside sorbitol normalization as a biomarker of AT-001 biological activity. There were approximately ten patients per cohort, with eight patients receiving AT-001 and two patients receiving placebo.

Pharmacokinetic Results

Even though the ER tablet did not release AT-001 from the polymer binding as expected, which resulted in low levels of exposure over a six-hour period, it aided in determining the lowest efficacious dose, as this cohort did not demonstrate a significant clinical response on the cardiac biomarker endpoints. The 1,500 mg BID and 1,000 mg TID capsule dosing regimens provided sustained levels of AT-001 in the bloodstream throughout the 24-hour period, but with different PK signatures. The figure below shows the PK profile of AT-001 in 1,500 mg BID and 1,000 mg TID rapid release capsule and the once daily ER tablet.

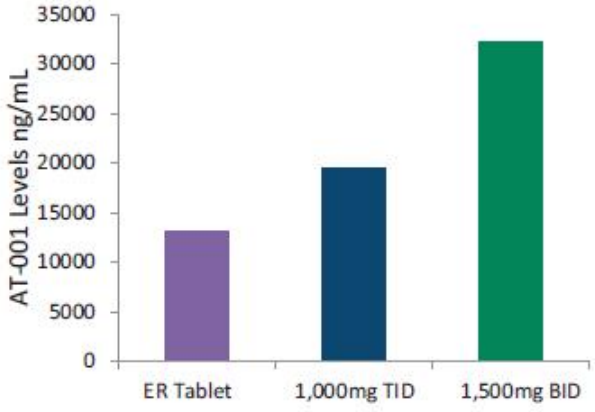
PK Profile of AT-001 over 24 Hours



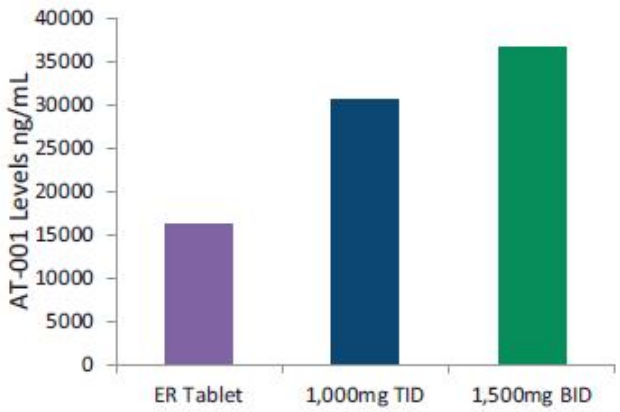
Additionally, as shown in the figures below, BID dosing regimen provided a slightly higher Cmax at first dose administration, with levels dropping low, but still above zero, at 12 hours post-dose. The TID dosing regimen provided a lower Cmax at the first dose, but displayed an additive effect after second dose administration to achieve a Cmax at the

second dose similar to that seen with the BID dosing regimen. Significant levels of AT-001 were sustained at all time-points with the TID dosing regimen.

AT-001 C_{max} (mean)



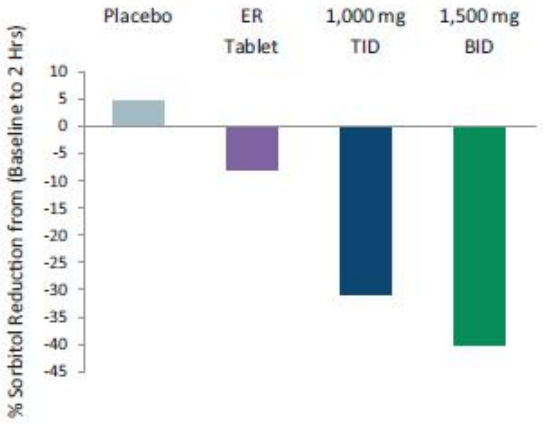
AT-001 AUC (mean)



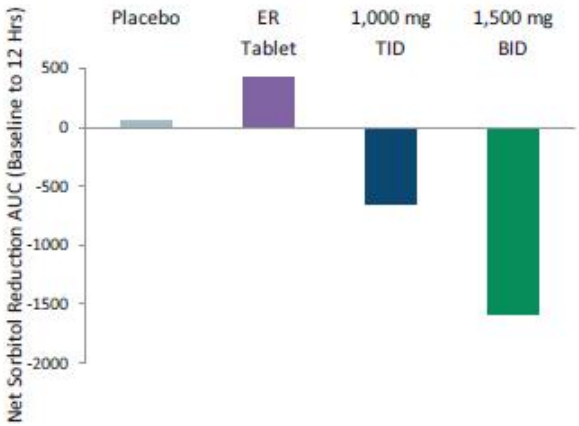
Sorbitol Reduction

As expected, due to the low exposure achieved with the ER tablet, only moderate sorbitol reduction was seen with the ER tablet as compared to the 1,500 mg BID and 1,000 mg TID rapid release capsule dosing regimens. However, both BID and TID capsule dosing regimens achieved the target range of sorbitol inhibition, normalizing sorbitol to that of healthy volunteers in many patients, and demonstrating statistically significant results versus placebo-treated patients at both two hours post-dose (Cmax) and when AUC was evaluated over 12 hours as shown in the figures below.

Sorbitol % Change at C_{max}



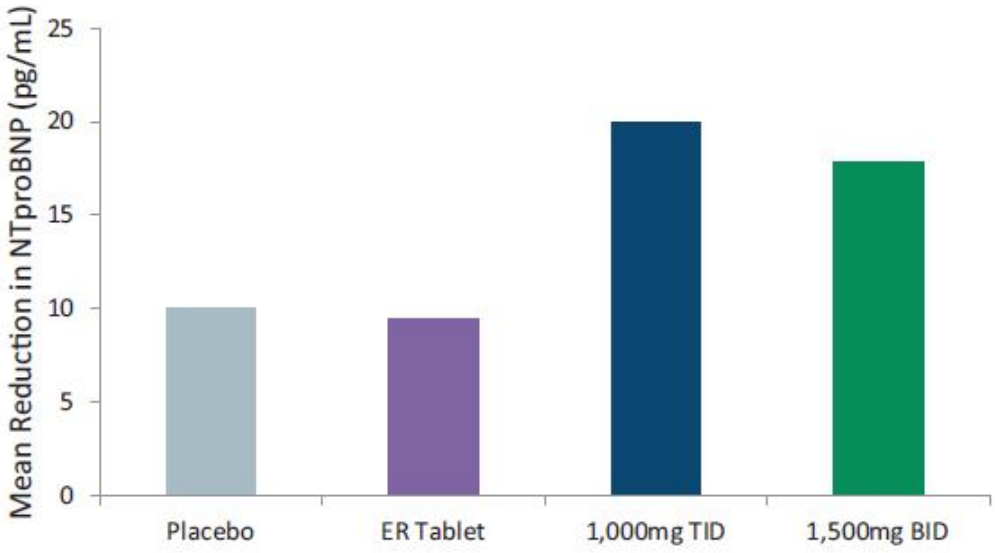
Sorbitol AUC 1-12h



NTproBNP Biomarker

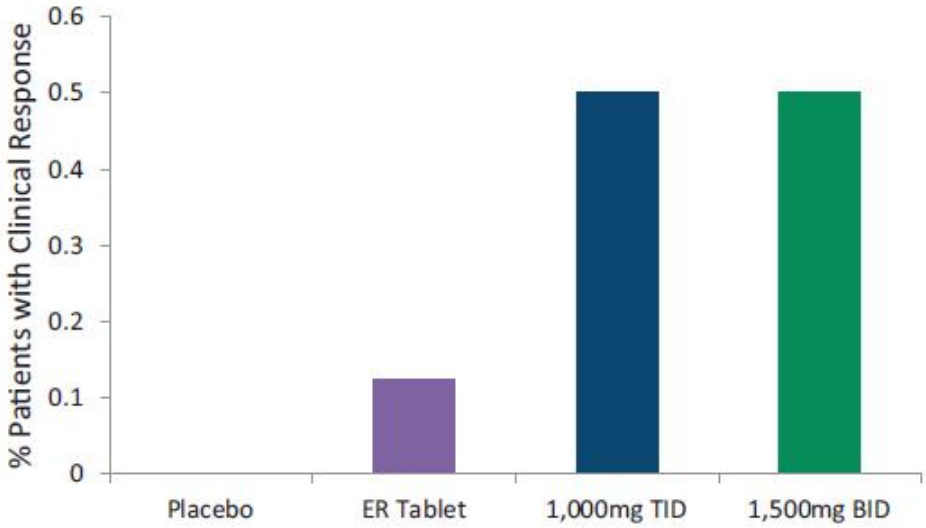
NTproBNP is a prohormone released by the heart in response to the stretching of the LV or changes in LV pressure. NTproBNP is well accepted as a blood-based biomarker of cardiac stress and function, and is used in the clinical setting to diagnose overt heart failure and acute myocardial infarction. Patients with early stage DbCM typically display lower levels of NTproBNP than patients with overt heart failure, but higher levels than non-DbCM diabetic patients or healthy volunteers. In diabetic patients, the level of NTproBNP prior to overt heart failure has been correlated with worsening cardiac outcomes over time. We hypothesized that by lowering the metabolic stress and damage to the heart caused by AR, AT-001 may affect NTproBNP levels in early stage DbCM patients. We demonstrated that treatment with AT-001 at 1,500 mg BID or 1,000 mg TID lowered mean NTproBNP levels across the cohort of treated patients over the 28-day treatment period versus placebo or the ER tablet. As shown in the figure below, both BID and TID treatment regimens displayed similar effects on NTproBNP, suggesting that the two different treatment regimens are similar in their effectiveness.

Change in NTproBNP 0-28 Days



Additionally, when NTproBNP levels were examined on an individual patient basis to assess the percent of patients that demonstrated a clinically meaningful reduction in NTproBNP, defined as a reduction of >25 pg/mL, the

BID and TID dose cohorts produced a greater percent of clinical responders versus placebo or ER tablet patients, as shown in the figure below.



Safety

AT-001 was well tolerated over 28 days at all doses and regimens tested. No serious adverse events or drug-related adverse events were reported over the 28-day treatment period, and no clinically significant abnormal lab values were noted.

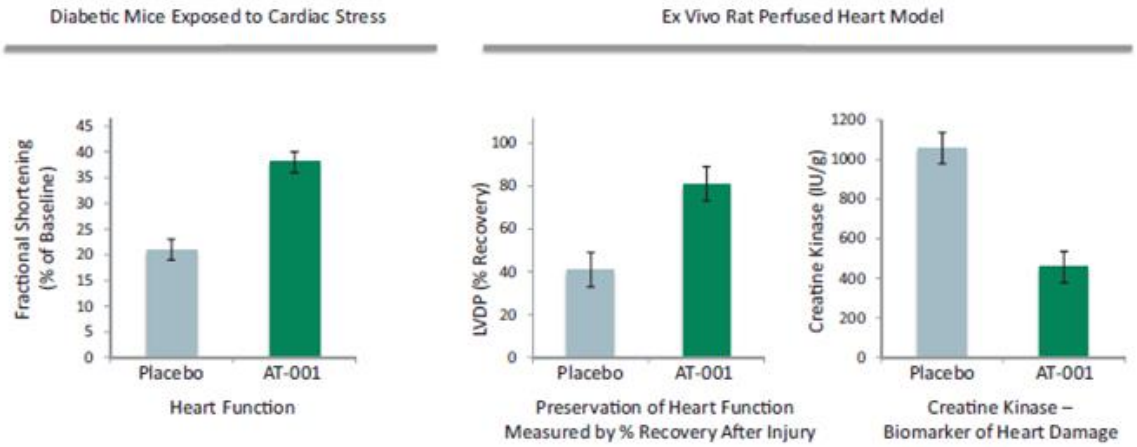
Preclinical Studies

In preclinical toxicology studies in dogs and rats, AT-001 was observed to be well tolerated up to 2,000 mg/kg per day, the maximum dose tested. No dose-limiting adverse effects or tolerability issues were observed. Additionally, no drug-related adverse effects were observed in hERG studies, micronucleus assays, Ames testing or any other preclinical safety and toxicology studies required for IND approval. Additionally, in vitro metabolism studies suggested that AT-001 is not significantly metabolized in hepatocytes and it does not inhibit cytochromes.

In preclinical efficacy studies in diabetic and non-diabetic rats and mice, AT-001 was cardioprotective, preventing damage caused by ischemia in the left anterior descending ligation model of cardiac damage. As shown in the

figures below, AT-001 in both pre-treatment and post-ischemia dosing models prevented cardiac damage, as measured by ischemic area, hemodynamic endpoints and biomarkers of heart damage.

AT-001 is Cardioprotective in Diabetic Models



Clinical Development Plan

Until recently, development in cardiovascular disease indications often required large outcome-based trials that examined survival and re-hospitalization as primary endpoints. These trials were extremely large, expensive and time-consuming, and were often confounded by comorbidities in the patient population. As a result, very few cardiovascular programs resulted in approved drugs. There has been a recent effort from the Division of Cardiovascular and Renal Products at the FDA, as well as at the European Medicines Agency, or EMA, to streamline drug development for cardiovascular disease to increase the probability of demonstrating a meaningful clinical effect in patients. Specifically in cardiomyopathies, where there is a direct functional link between hemodynamic endpoints, heart contractility and quality of life, there is a unique opportunity to demonstrate benefit of therapy in a smaller number of patients and shorter treatment period than was previously required. Recent clinical development programs in hereditary cardiomyopathies have pioneered smaller trials examining exercise tolerance and/or heart functional class as a primary endpoint. Based on this precedent, we plan to take a similar approach to development of AT-001 for the treatment of DbCM.

Consistent with these developments, at our pre-IND meeting, the FDA indicated that we would not be required to examine survival and re-hospitalization endpoints, and confirmed that exercise tolerance would qualify as an appropriate primary endpoint in our DbCM trial. This was also recently publicly confirmed by the FDA in a whitepaper entitled “Draft Guidance for Industry: Treatment for Heart Failure: Endpoints for Drug Development.” Accordingly, we designed our pivotal Phase 2/3 clinical trial to target functional capacity, or exercise tolerance, as measured by Peak VO2 on Cardiopulmonary Exercise Testing (CPET) in DbCM patients at high risk of progression to overt heart failure. The primary endpoint in the trial will be stabilization or decrease in slope of decline on functional capacity, as measured by peak VO2, the rate of oxygen consumption measured during exercise. We are also evaluating heart function by echocardiogram-based hemodynamic endpoints, progression to overt heart failure, and quality of life, as well as biomarkers of heart inflammation and damage. This trial will consist of 675 patients in three cohorts of approximately 225 patients each, including a placebo group, a low dose AT-001 group (1,000mg twice daily) and a high dose AT-001 group (1,500mg twice daily). The trial treatment period for evaluation of the primary endpoint will be 15 months, with additional endpoints evaluated at 27 months. In September 2019, we announced the initiation of a Phase 3 registrational trial for AT-001 in DbCM called ARISE-HF.

AT-001 for the Treatment of Diabetic Peripheral Neuropathy

Overview

We also intend to develop AT-001 for DPN, a debilitating neurodegenerative disease that significantly reduces patients' quality of life, and for which there are currently no FDA-approved treatments. We expect this indication will require a standard clinical development path, and as such we plan to pursue a strategic partnership in order to expand into this indication. Since many patients with DbCM also have DPN, we plan to collect proof-of-concept data through our DbCM program to support our efforts in our DPN program. We have included a DPN sub-study in our pivotal DbCM study.

Diagnosis and Current Standard of Care

DPN is diagnosed by a simple neurological assessment, usually the Toronto Neuropathy Scoring System, which is administered in the physician's office and examines a patient's ability to feel various types of neurological stimuli on the hands and feet. AR activity has been shown to cause DPN. Epalrestat, an ARI, is approved in Japan, China and India to prevent further neuronal degeneration in DPN patients. However, there are no disease modifying therapies approved in the United States and Europe, and only symptomatic medications, such as Lyrica, are approved for pain associated with DPN. Although epalrestat was approved in Japan in 1992 based on very limited clinical data that would not have been sufficient for other markets, more recent academic studies have demonstrated an effect on MNCV and symptomatic pain endpoints in a wide range of diabetic patients. For example, a multicenter, three-year Phase 3 clinical trial conducted in Japan on epalrestat 150 mg versus placebo demonstrated that epalrestat prevented progression of DPN in diabetic patients versus placebo. Epalrestat prevented degeneration of nerve function, as measured by MNCV, and prevented worsening of symptomatic pain. A statistically significant effect was demonstrated in all patients regardless of low or high levels of glucose attached to their hemoglobin, as tested by a hemoglobin A1C (HbA1C) test.

Epalrestat, which is now generic in Japan, reached peak sales of approximately $226 million in 2001. This is indicative of its widespread use in the Japanese diabetic population, which was approximately five million patients at the time of launch despite significant tolerability issues associated with use and five times daily dosing due to a very short half-life. We do not believe, however, that it is likely to be a candidate for further commercialization. Nevertheless, prior research on epalrestat evinces the role of AR in DPN and provides a clinical trial design to demonstrate efficacy in this indication.

Market Opportunity

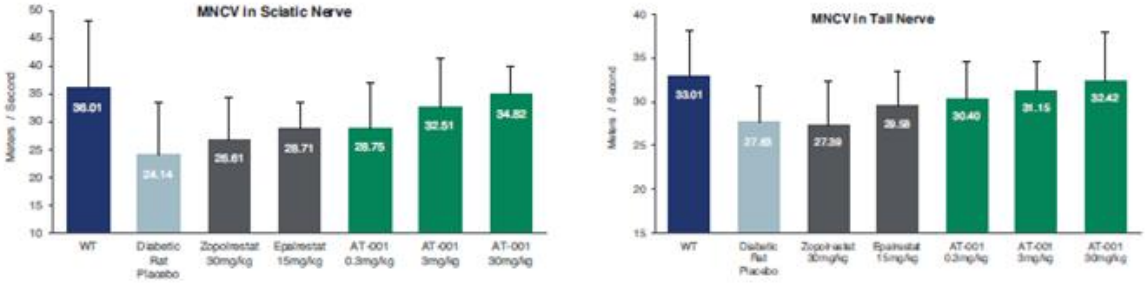
Approximately 50% of the global diabetic population, or 226 million diabetic patients, suffer from DPN, with 23.0 million patients in North America and 29.0 million patients in Europe. Due to availability of generic epalrestat in China and India, we view the opportunity in these two markets to be limited as a result of pricing pressures and differentiation requirements with regard to epalrestat. However, we believe a significant market opportunity for a more effective ARI with a favorable dosing regimen still exists in Japan, a less price sensitive market where there is familiarity with the mechanism of action in the disease and use of epalrestat is high. As such, although we are currently focused on the U.S. market, we may expand our efforts into Japan opportunistically.

Preclinical Studies

In preclinical studies, AT-001 demonstrated improvements in neuronal degeneration in animal models of DPN and provided good exposure to peripheral nerve tissue, as measured by MNCV in sciatic and tail nerves of diabetic rats. As shown in the figures below, in a type 1 diabetic rat model of peripheral neuropathy, AT-001 treatment prevented peripheral neuronal damage, as measured by MNCV after six weeks of treatment with zopolrestat 30 mg/kg, epalrestat 15 mg/kg, AT-001 0.3 mg/kg, 3 mg/kg or 30 mg/kg, or placebo. The diabetic rats treated with placebo demonstrated a reduction in nerve function as measured by MNCV versus non-diabetic wild-type, or WT, rats, confirming that the six weeks of diabetes duration caused neuronal dysfunction. A dose-dependent reduction in neuronal dysfunction was observed in rats treated with AT-001, and treatment at 30 mg/kg of AT-001 completely prevented neuronal

degeneration, with no statistical difference from non-diabetic WT rats. Effects of treatment with AT-001 demonstrated a similar effect versus zopolrestat or epalrestat at lower doses, and an increased effect at higher doses.

Induced Diabetic Rat Models (Six-Week Treatment)



In a type 2 diabetic rat model, AT-001 demonstrated improvements in neuronal degeneration versus epalrestat. Zucker diabetic fatty, or ZDF, rats were treated with epalrestat 30 mg/kg, AT-001 1 mg/kg, 3 mg/kg or 10 mg/kg, or placebo for 12 weeks, and effects on neurons were measured by MNCV. The diabetic rats treated with placebo demonstrated a reduction in nerve function as measured by MNCV versus non-diabetic WT rats, confirming that the 12 weeks of diabetes duration caused neuronal dysfunction. Treatment with AT-001 showed a dose-dependent reduction in neuronal dysfunction, and treatment at 10 mg/kg completely prevented neuronal degeneration, with no statistical difference from non-diabetic WT rats. Effects of treatment with AT-001 demonstrated a similar effect versus epalrestat at a varying dose of 30 mg/kg of epalrestat versus 3 mg/kg of AT-001, and an increased effect at 1/3 the dose of 30 mg/kg of epalrestat versus 10 mg/kg of AT-001.

Clinical Development Plan

Since many DbCM patients often also suffer from DPN, we have incorporated DPN endpoints, such as MNCV, as a sub-study into our DbCM pivotal program to provide additional proof-of-concept for AT-001 in DPN. We plan to seek a strategic partnership to develop AT-001 for treatment of DPN and advance the program into Phase 3 clinical trial for this indication.

AT-003 for the Treatment of Diabetic Retinopathy

Overview

We are developing AT-003, an ARI designed to cross through the back of the eye when dosed orally, which has demonstrated strong retinal penetrance, for the treatment of DR. DR is an ophthalmic disease that occurs in diabetic patients, and for which treatments are currently limited to intravitreal administration. DR has been linked to AR activity, including elevations in sorbitol and subsequent changes in retinal blood vessels, which distorts vision and leads to permanent blindness. We are currently in late stages of preclinical development and intend to advance AT-003 into a Phase 1 clinical trial for the treatment of DR in 2020.

Diagnosis and Current Standard of Care

DR is diagnosed by routine dilated eye exam by an ophthalmologist. Annual or biennial ophthalmic exams to screen for DR are a recommended standard of care for diabetic patients under current treatment guidelines. Vascular endothelial growth factor, or VEGF, inhibitors, Lucentis (ranibizumab) and Eylea (aflibercept), are approved to treat severe or late-stage DR, but are limited by high cost, the need for intravitreal injection into the eye and the lack of therapeutic benefit in many patients. A need exists for safe, effective and tolerable treatments for DR early in the disease process that provide a benefit to a wide range of patients. AR is an attractive target for DR drug development since AR activity is upstream of VEGF activity in DR pathogenesis. AR has been shown to cause DR by inducing hyperosmolarity

in retinal cells due to elevated sorbitol, as well as through fructose-mediated detrimental downstream effects, such as AGE generation and PKC activation. AR knock-out rats are protected from DR development, and several prior ARIs demonstrated efficacy on DR endpoints in clinical trials, but were not approved due to dose-limiting safety concerns.

Market Opportunity

A recent retrospective epidemiological analysis of diabetic patients globally confirmed that DR affects approximately 35% of diabetics, and is a leading cause of blindness worldwide. Based on the 2017 diabetes numbers, the global market for DR is approximately 158 million patients, with anticipated increase to 243 million by 2045. The current market is approximately 16.0 million in North America and 20.0 million in Europe.

Preclinical Studies

AT-003 displayed significant retinal penetration when dosed orally in diabetic rats. AT-003 was observed to be well tolerated over a seven-day dosing period in all doses tested, up to 1,000 mg/kg daily, with no adverse effects observed. Efficacy of AT-003 is currently being explored in two animal models of DR — an ischemic injury model (acute damage) and chronic diabetic treatment model.

Clinical Development Plan

Similar to AT-001, we plan to explore the safety, tolerability, PK profile and biomarker effects of AT-003 in a Phase 1a/1b clinical trial in diabetic patients. Assuming positive data in this trial, we plan to initiate a pivotal Phase $^{2}/_{3}$ clinical trial of AT-003 in patients with DR to prevent disease progression versus placebo, as measured by subjective metrics, including fluoroscein angiography and optical coherence tomography, which are scans used in the examination and management of retinal diseases.

Our Early-Stage PI3K Program

PI3 kinkases, or PI3K, are a family of membrane-based enzymes containing a catalytic subunit that exists in four different isoforms: alpha, beta, delta and gamma. PI3K triggers a signaling cascade that regulates cell proliferation and survival, and is constitutively activated in many tumor cell lines. Prior PI3K inhibitors were nonselective for subunit inhibition, and were plagued by tolerability and safety issues, such as hepatic toxicity, severe diarrhea and colitis, hyperglycemia and hypertension, which are believed to be due to inhibition of the alpha and beta subunits. Selective inhibition of certain PI3K subunits may be advantageous in targeting tumor cells and maximizing response, while avoiding dose-limiting side effects and tolerability issues. Using similar strategies to our ARI program, we have developed highly selective PI3K inhibitors that target the delta subunit, as well as dual delta/gamma selectivity.

AT-104 for the Treatment of Orphan Hematological Oncology

We expect to initially target orphan hematological oncology indications, including peripheral T-cell lymphoma, cutaneous T-cell lymphoma and T-cell acute lymphoblastic leukemia. We plan to initiate our clinical program in these indications in 2021. We are additionally developing selective alpha/gamma inhibitors to target solid tumors that constitutively express PI3K alpha.

Exclusive License Agreement with Columbia University

On October 26, 2016, we entered into a license agreement with Columbia University (the “2016 Columbia Agreement”). Pursuant to the 2016 Columbia Agreement, Columbia University granted us a royalty-bearing, sublicensable license that is exclusive with respect to certain patents, and non-exclusive with respect to certain know-how, in each case to develop, manufacture, and commercialize ARI products, including AT-001, AT-003 and AT-007. The license grant is worldwide with the exception of a single patent family covering AT-001 and AT-003 for which the license grant excludes China, Taiwan, Hong Kong and Macao. Under the 2016 Columbia Agreement, we are obligated to use commercially reasonable efforts to research, discover, develop and market licensed products for commercial sale in the licensed territory, and to comply with certain obligations to meet specified development and

funding milestones within defined time periods. Columbia University retains the right to conduct, and grant third parties the right to conduct, non-clinical academic research using the licensed technology; *provided* that such research is not funded by a commercial entity or for-profit entity or results in rights granted to a commercial or for-profit entity. As the technology licensed to us under the 2016 Columbia Agreement was developed as a result of a U.S. government grant, the licenses granted to us under the agreement are subject to the terms of such grant, and to standard rights of the U.S. government under the Bayh-Dole Act, including the grant to the government of a non-exclusive, worldwide, freedom to operate license under any patents, and the requirement, absent a waiver, to manufacture products substantially in the United States.

As consideration for entering into the 2016 Columbia Agreement, we made a nominal upfront payment to Columbia University and, following the occurrence of certain trigger events, issued to Columbia University shares equal to 5% of our outstanding common stock on a fully diluted basis at the time of issuance. We will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2016 Columbia Agreement. We will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on our, our affiliates' and our sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, we are required to make specified annual minimum royalty payments to Columbia University in the mid six figures beginning on the 10th anniversary of the effective date of the agreement. As of the date of this Annual Report on Form 10-K, we have not granted any sublicenses under the 2016 Columbia Agreement. However, if we sublicense the rights granted under the 2016 Columbia Agreement to one or more third parties, we will be required to pay to Columbia University a portion of the net sublicensing revenue received from such third parties, at percentages between 10% and 20%, depending on the stage of development at the time such revenue is received from such third parties.

Columbia University is responsible for the prosecution and maintenance of the licensed patents, in consultation with us, and subject to a requirement to give due consideration to our comments, at our expense. We have the first right, but not the obligation, to control the enforcement of licensed patents exclusively licensed to us against third parties. We are required to indemnify Columbia University for any third party claims that arise from or relate to the 2016 Columbia Agreement.

The 2016 Columbia Agreement will terminate upon the expiration of all our royalty payment obligations in all countries. We may terminate the 2016 Columbia Agreement for convenience upon 90 days' written notice to Columbia University. At its election, Columbia University may terminate the 2016 Columbia Agreement, or convert the licenses granted to us into non-exclusive, non-sublicensable licenses, in the case of (a) our uncured material breach upon 30 days' written notice (which shall be extended to 90 days if we are diligently attempting to cure such material breach), (b) our failure to achieve the specified development and funding milestone events, or (c) our insolvency. The 2016 Columbia Agreement may not be assigned by us without Columbia University's consent, except to any successor to all or substantially all of our business to which the 2016 Columbia Agreement relates and upon notice to Columbia University.

In January 2019, the Company entered into a second license agreement with Columbia University (the "2019 Columbia Agreement"). Pursuant to the 2019 Columbia Agreement, Columbia University granted the Company a royalty-bearing, sublicensable license that is exclusive with respect to certain patents, and non-exclusive with respect to certain know-how, in each case to develop, manufacture and commercialize PI3k inhibitor products. The license grant is worldwide. Under the 2019 Columbia Agreement, the Company is obligated to use commercially reasonable efforts to research, discover, develop and market licensed products for commercial sale in the licensed territory, and to comply with certain obligations to meet specified development and funding milestones within defined time periods. Columbia University retains the right to conduct, and grant third parties the right to conduct, non-clinical academic research using the licensed technology; provided that such research is not funded by a commercial entity or for-profit entity or results in rights granted to a commercial or for-profit entity. As consideration for entering into the 2019 Columbia Agreement, the Company made a nominal upfront payment to Columbia University. The Company will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2019 Columbia Agreement. The Company will

also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on the Company's, its affiliates' and its sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, the Company is required to make specified annual minimum royalty payments to Columbia University, which is contingent upon the approval of the licensed products, in the mid-six figures beginning on the tenth anniversary of the effective date of the 2019 Columbia Agreement.

The Company has not granted any sublicenses under the 2019 Columbia Agreement. However, if the Company sublicenses the rights granted under the 2019 Columbia Agreement to one or more third parties, it will be required to pay Columbia University a portion of the net sublicensing revenue received from such third parties, at percentages between 10% and 50%, depending on the stage of development at the time such revenue is received from such third parties. The 2019 Columbia Agreement will terminate upon the expiration of all the Company's royalty payment obligations in all countries. The Company may terminate the 2019 Columbia Agreement for convenience upon 90 days' written notice to Columbia University. At its election, Columbia University may terminate the 2019 Columbia Agreement, or convert the licenses granted to the Company into non-exclusive, non-sublicensable licenses, in the case of (a) the Company's uncured material breach upon 30 days' written notice (which shall be extended to 90 days if the Company is diligently attempting to cure such material breach), (b) the Company's failure to achieve the specified development and funding milestone events, or (c) the Company's insolvency.

In March 2019, and in connection with the 2016 Columbia Agreement, we entered into a research services agreement (the "2019 Columbia Research Agreement") with Columbia University with the purpose of analyzing structural and functional changes in brain tissue in an animal model of galactosemia, and the effects of certain compounds whose intellectual property rights were licensed to us as part of the 2016 Columbia Agreement on any such structural and functional changes. The 2019 Columbia Research Agreement has a term of 12 months from its effective date; *provided* that we can terminate the 2019 Columbia Research Agreement without cause with at least 30 days' prior written notice. The services covered by the 2019 Columbia Research Agreement will be performed by Columbia University in two parts (Part 1 and Part 2) of six months each. The decision to proceed with Part 2 of the 2019 Columbia Research Agreement shall be made solely by us and will be contingent on the success of the research performed in Part 1. In consideration for the services performed by Columbia University in Part 1, we will be required to pay $0.1 million to Columbia University for staffing, supplies and indirect costs. If we decide to continue the research defined in Part 2, we will be required to pay an additional $0.2 million to Columbia University. To the extent new intellectual property is developed under the 2019 Columbia Research Agreement that we elect to license from Columbia University, we may be required to pay Columbia University additional consideration for such rights. The 2019 Columbia Research Agreement may not be assigned by us without Columbia University's consent, except to any successor to all or substantially all of our business to which the 2019 Columbia Research Agreement relates or to an affiliate, in each case upon notice to Columbia University.

On October 3, 2019, and in connection with the 2019 Columbia Agreement, the Company entered into a research services agreement (the "PI3k Columbia Research Agreement" and collectively with the 2016 Columbia Agreement, 2019 Columbia Agreement and 2019 Research Agreement, the "Columbia Agreements") with Columbia University with the purpose of analyzing PI3k inhibitors for the treatment of lymphoid malignancies. The research service agreement has a term of 18 months from is effective date; provided that the Company can terminate the research service agreement without cause with at least 30 days prior written notice. Midway through the study period, the Company and Columbia University will review the results of all completed and in progress research and determine whether the research will continue. In consideration for the services performed by Columbia University, the Company will be required to pay $0.4 million to Columbia University for staffing, supplies and indirect costs.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We intend to build a commercial infrastructure to support sales of our product candidates in the United States. We expect to manage sales, marketing and distribution through internal resources and third party relationships. While we may commit significant financial and management resources to commercial activities, we will also consider collaborating with one or more pharmaceutical companies to enhance our commercial capabilities. Outside the United States, we plan to seek pharmaceutical partners for sales and marketing activities.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We depend on third party contract manufacturing organizations, or CMOs, for all of our requirements of raw materials, drug substance and drug product for our preclinical research and our clinical trials for AT-001, AT-007 and AT-003. We have not entered into long-term agreements with our current CMOs. We intend to continue to rely on CMOs for later-stage development and commercialization of our current products, as well as the development and commercialization of any other product candidates that we may identify. Although we rely on CMOs, we have personnel and third party consultants with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

We believe the synthesis of the drug substance for AT-001 and AT-007 are reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale production and do not require unusual equipment or handling in the manufacturing process. We have obtained adequate supplies of the drug substance for AT-001 and AT-007 to satisfy our immediate clinical and preclinical demands.

Drug product formulation development for AT-001 is in progress. We have contracted with a third party manufacturer capable of both formulation development and drug product manufacturing through commercialization. We may identify a second drug product manufacturer in the future to add additional capacity and redundancy to our supply chain. In our completed Phase 1 SAD/MAD clinical trial of AT-001, we developed and utilized a rapid release capsule formulation filled with API powder. AT-007 is dosed as a powder in a capsule for adult treatment, and we will develop a dose suspension formulation for future pediatric treatment.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, the expertise of our executive and scientific team, research, clinical capabilities, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

There are currently no therapies approved to treat DbCM. Entresto, a drug developed by Novartis International AG, or Novartis, is approved for acute heart failure, which can be caused by many conditions, including DbCM. However, we are aware that Novartis may be pursuing a label expansion for earlier treatment of generalized heart failure, which may overlap with our target disease stages in DbCM. Additionally, sponsors of sodium-glucose cotransporter-2, or SGLT2, inhibitors are pursuing broad cardiovascular labels in type 2 diabetes patients, which may include a subset of DbCM patients as part of the larger diabetic population at risk for heart failure. We are also aware of planned Phase 2 clinical trials on glucagon-like peptide-1, or GLP-1, agonists in DbCM, as well as anti-fibrotic therapies in Phase 1 clinical development. Many of these programs are sponsored by large pharmaceutical companies with a strong presence in cardiology and metabolic disease. Additionally, stem-cell targeted initiatives are in various stages of preclinical and early clinical development to stimulate regeneration of cardiac tissue to counter fibrosis in DbCM. There have been prior studies demonstrating effectiveness in DbCM of off-label use of sildenafil, although we do not believe this represents a commercially viable competitive threat.

There are no disease modifying therapies approved to treat DPN outside of Japan, India and China. In these limited markets, epalrestat, another ARI, is approved to prevent worsening of DPN, and despite challenges in compliance due to frequent dosing three to five times daily, the drugs are generic and offer a low cost alternative. A more effective therapy with improved tolerability and dosing may offer an advantage. A re-formulation of proprietary crystalline epalrestat, BNV-222, is in development for DPN in Russia in a 12-month Phase $^{2}/_{3}$ clinical trial, which completed enrollment in 2016, but has not yet reported any results.

There are currently no therapies approved to treat galactosemia. Due to the importance of GALK and GALT enzymes within neurons in the CNS, we believe that enzyme replacement therapy is not an effective approach in this indication. Additionally, numerous mutations across ethnicities are responsible for loss of function in GALK or GALT, which presents significant challenges to potential gene editing approaches.

There are several therapies approved to treat severe or late-stage forms of DR, or proliferative DR, such as diabetic macular edema and proliferative DR, including anti-VEGF therapies, Lucentis and Eylea, which represents approximately 20% of the larger DR population. There are currently no therapies approved to treat non-proliferative DR, an earlier stage of the disease upstream of vessel or capillary proliferation. However, there are significant additional clinical development efforts for other mechanistic interventions in early-stage or for non-proliferative DR.

The following table summarizes the current competitive landscape for our initial target indications:

Disease	Product Type	Stage of Development
DbCM	Entresto (sacubitril/valsartan)	Approved for late stages of generalized cardiac heart failure; may pursue earlier stages of heart failure that may overlap with DbCM
	SGLT2 inhibitors	Approved for glucose control with additional label claiming cardiovascular benefit in diabetics; may achieve specific label in DbCM in future studies
	GLP-1 agonists	Approved; additional studies examining direct CV benefit in DbCM anticipated
	Anti-fibrotic therapies	Preclinical to Phase 1; may prevent collagen cross-linking and B-catenin remodeling
DPN	Epalrestat (ARI);	Approved as a generic in Japan, China and India
	BNV-22 epalrestat reformulation	Attempt to reformulate as a novel product in Russia in Phase 2/3 trial (no information available since 2016)
Galactosemia		None identified
DR	Anti-VEGFs (Lucentis; Eylea)	Approved for proliferative forms of DR—only 20% of DR population
	Other mechanisms	Phase 2a development for non-proliferative DR

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, new therapeutic approaches and potential indications, and other inventions that are important to our business. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important for the development and implementation of our business. We also rely on the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how that is not patentable, we rely on confidentiality agreements to protect our interests. We require our employees, consultants and advisors to enter into confidentiality agreements prohibiting the disclosure of confidential information and requiring disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Our patent portfolio includes patents and patent applications that are exclusively licensed from Columbia University and patent applications that are owned by us. Our patent portfolio includes patents and patent applications that cover our product candidates AT-001, AT-003, AT-007 and AT-104, and the use of these candidates for therapeutic

purposes in certain territories. Our proprietary technology has been developed primarily through relationships with academic research centers and contract research organizations.

For our product candidates, we will, in general, initially pursue patent protection covering compositions of matter and methods of use. Throughout the development of our product candidates, we seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including through additional methods of use, process of making, formulation and dosing regimen-related claims.

In total, our patent portfolio, including patents licensed from Columbia University and patents owned by us, comprises eight different patent families, filed in various jurisdictions worldwide, including families directed to composition of matter for AR inhibitors, and a family directed to methods of treating galactosemia and complications associated with galactosemia using AR inhibitors. Our patent portfolio includes issued patents in the United States, Europe, Japan, Australia and Canada. Our patent portfolio is outlined below:

Composition of Matter Patents

AT-001 and AT-003. As of January 10, 2020, we have exclusively licensed from Columbia University a patent family that includes three issued patents in the United States, 44 issued patents in Europe, Japan, Canada and Australia, two pending applications in the United States that claim the composition of matter of and certain methods of use with respect to AT-001 and AT-003. The 20-year term of the patents in this family runs through July 2031, absent any available patent term adjustments or extensions.

AT-007. We have exclusively licensed a patent family from Columbia University that includes an issued composition of matter patent in the United States and a pending European patent application that claim the composition of matter of and certain methods of use with respect to AT-007. In addition, we have also filed applications in Japan, China, Canada, Australia, Russia, Brazil, India, Israel, Mexico, New Zealand, Singapore, South Africa and Hong Kong. The 20-year term of patents in this family runs through June 2037, absent any available patent term adjustments or extensions.

AT-104. We have exclusively licensed an early-stage patent family from Columbia University that currently includes one pending international patent application filed under the Patent Cooperation Treaty, or PCT, that claims the composition of matter of and certain methods of use with respect to AT-104. We intend to file national phase applications based on this PCT application before applicable deadlines. The 20-year term of any patents in this family that may issue will run through July 2038, absent any available patent term adjustments or extensions.

Methods for Treating Galactosemia

We own a pending PCT patent application that claims methods for treating galactosemia and preventing complications associated with galactosemia using AT-007 and other inhibitors of AR. We plan to file national stage applications in the United States, Europe and other jurisdictions before the deadlines to file such applications. No patents have issued to date, but we expect that the 20-year term of patents that do issue in this family will run through July 2038, absent any available patent term adjustments or extensions.

We expect to file future patent applications on innovations that are developed in the course of advancing our pipeline through preclinical and clinical development.

Patent Term and Term Extensions

Individual patents have terms for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, utility patents issued for applications filed in the United States are granted a term of 20 years from the earliest effective filing date of a non-provisional patent application. In addition, in certain instances, the term of a U.S. patent can be extended to recapture a portion of the United States Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA

component, the restoration period cannot be longer than five years and the restoration period cannot extend the patent term beyond 14 years from FDA approval. In addition, only one patent applicable to an approved drug is eligible for the extension, and only those claims covering the approved drug, a method for using it, or a method of manufacturing may be extended. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. All taxes, annuities or maintenance fees for a patent, as required by the USPTO and various foreign jurisdictions, must be timely paid in order for the patent to remain in force during this period of time.

The actual protection afforded by a patent may vary on a product by product basis, from country to country, and can depend upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions and the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Our patents and patent applications may be subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled “Risk Factors — Risks Related to Our Intellectual Property.”

Trademarks and Know-How

In connection with the ongoing development and advancement of our products and services in the United States and various international jurisdictions, we seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate. In addition to patent and trademark protection, we rely upon know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by using confidentiality agreements with our commercial partners, collaborators, employees and consultants, and invention assignment agreements with our employees and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed by our employees and through relationships with third parties. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors, commercial partners, collaborators, employees, and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, see the section titled “Risk Factors — Risks Related to Our Intellectual Property.”

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local levels, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products, such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources.

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory 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 drug development process, approval process or after approval, may subject an applicant to delays and a variety of administrative or judicial sanctions, such as the FDA’s refusal to approve a pending New Drug Application, or NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product

seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials, in accordance with good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of an FDA inspection of selected clinical sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold or a partial clinical hold.

In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that

institution, and the IRB must continue to oversee the clinical trial while it is being conducted and reapprove the study at least annually. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In Phase 1, the drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In Phase 2, the drug typically is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. In Phase 3, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the safety and efficacy of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted, at least annually, to the FDA, and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions, findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product, and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements, or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes 12 months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. The FDA may further extend the review process for three additional months to consider new information provided by the applicant to address any outstanding deficiency identified by the FDA following the original submission.

In addition, under the Pediatric Research Equity Act, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the

additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP requirements.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and takes several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval of an NDA on a timely basis, or at all.

After evaluating the NDA 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 in order for 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 will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If the FDA approves a sponsor's marketing application for a designated orphan drug for use in the rare disease or condition for which it was designated, the sponsor is eligible for a seven-year period of marketing exclusivity, during which the FDA may not approve another sponsor's marketing application for a drug with the same active moiety and intended for the same use or indication as the approved orphan drug, except in limited circumstances, such as if a subsequent sponsor demonstrates its product is clinically superior. During a sponsor's orphan drug exclusivity period, competitors, however, may receive approval for drugs with different active moieties for the same indication as the approved orphan drug, or for drugs with the same active moiety as the approved orphan drug, but for different indications. Orphan drug exclusivity could block the approval of one of our product candidates for seven years if a competitor obtains approval for a drug with the same active moiety intended for the same indication before we do, unless we are able to demonstrate that grounds for withdrawal of the orphan drug exclusivity exist, such as that our product is clinically superior. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, priority review, accelerated approval and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted. The FDA may do so if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that are designed to treat serious conditions, and if approved, would provide a significant improvement in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Under the current PDUFA agreement, these six and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

Rare pediatric disease, or RPD, designation by the FDA enables priority review voucher, or PRV, eligibility upon U.S. market approval of a designated drug for rare pediatric diseases. The RPD-PRV program is intended to encourage development of therapies to prevent and treat rare pediatric diseases. The voucher, which is awarded upon NDA or Biologics License Application, or BLA, approval to the sponsor of a designated RPD can be sold or transferred to another entity and used by the holder to receive priority review for a future NDA or BLA submission, which reduces the FDA review time of such future submission from ten to six months.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval. To qualify, the FDA must determine that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform

post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

Breakthrough therapy designation is for a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. We may explore some of these opportunities for our product candidates as appropriate.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims, are subject to further testing requirements and prior FDA review and approval. There also are continuing annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as application fees for supplemental applications with clinical data.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance.

The FDA may also subject a drug to official lot release, which requires manufacturers to submit several items to the FDA with respect to each lot of a drug before it is released to distribution. These items include samples of each lot, a summary of the manufacturing history of the lot and the results of any tests performed on the lot.

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 reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or

clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications. The FDA and other agencies actively enforce the laws and regulations prohibiting their promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Federal and State Fraud and Abuse, Data Privacy and Security, and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws and regulations restrict business practices in the biopharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities and proposed sales, marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers and other parties through which we may market, sell and distribute any products for which we obtain marketing approval. These laws include anti-kickback and false claims laws and regulations, data privacy and security, and transparency laws and regulations, including, without limitation, those laws described below.

The federal Anti-Kickback Statute prohibits any person or entity from, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting

from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act or the civil monetary penalties laws.

Federal civil and criminal false claims laws and civil monetary penalties laws, including the federal civil False Claims Act, which can be enforced by individuals through civil whistleblower or qui tam actions, prohibits any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose specified requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain healthcare providers, healthcare clearinghouses and health plans, that create, receive, maintain or transmit individually identifiable health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which are not pre-empted by HIPAA, differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state and local laws that require the registration of pharmaceutical sales representatives. State legislatures are increasingly focused on pharmaceutical company activities, and we may be subject to additional new state or federal legislative requirements in the future that could impact our ability to commercialize our product candidates, if they are approved.

Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant criminal, civil and administrative penalties

including damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, disgorgement, exclusion from participation in government healthcare programs and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates 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, implementation of corporate compliance programs, reporting of payments or transfers of value to healthcare professionals, and additional data privacy and security requirements.

Coverage and Reimbursement

The future commercial success of our product candidates, if approved, will depend in part on the extent to which third party payors, such as governmental payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers and other third party payors, provide coverage of and establish adequate reimbursement levels for our product candidates. Third party payors generally decide which products they will pay for and establish reimbursement levels for those products. In particular, in the United States, no uniform policy for coverage and reimbursement exists. Private health insurers and other third party payors often provide coverage and reimbursement for products based on the level at which the government, through the Medicare program, provides coverage and reimbursement for such products, but also on their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement can differ significantly from payor to payor.

In the United States, the European Union, or EU, and other potentially significant markets for our product candidates, government authorities and third party payors are increasingly attempting to limit or regulate the price of products, particularly for new and innovative products, which often has resulted in average selling prices lower than they would otherwise be. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage. These pressures can arise from rules and practices of managed care groups, judicial decisions and laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical coverage and reimbursement policies and pricing in general.

Third party payors are increasingly imposing additional requirements and restrictions on coverage and limiting reimbursement levels for products. For example, federal and state governments reimburse products at varying rates generally below average wholesale price. These restrictions and limitations influence the purchase of products. Third party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Third party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of products, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third party payor reimbursement may not be available to enable us to realize an appropriate return on our investment in product development. Legislative proposals to reform healthcare or reduce costs under government insurance programs may result in lower reimbursement for our product candidates, if approved, or exclusion of our product candidates from coverage and reimbursement. The cost containment measures that third party payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates.

Healthcare Reform

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates. The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates profitably, if approved. Among policy makers and payors in the United States and

elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts, which include major legislative initiatives to reduce the cost of care through changes in the healthcare system, including limits on the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded healthcare programs, and increased governmental control of drug pricing.

There have been several U.S. government initiatives over the past few years to fund and incentivize certain comparative effectiveness research, including creation of the Patient-Centered Outcomes Research Institute under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates.

The PPACA became law in March 2010 and substantially changed the way healthcare is financed by third party payors, and significantly impacts the U.S. pharmaceutical industry. Among other measures that may have an impact on our business, the PPACA establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; a new Medicare Part D coverage gap discount program; and a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Additionally, the PPACA extends manufacturers' Medicaid rebate liability, expands eligibility criteria for Medicaid programs, and expands entities eligible for discounts under the Public Health Service Act. At this time, we are unsure of the full impact that the PPACA will have on our business.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the PPACA, and we expect such challenges and amendments to continue. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain PPACA provisions or otherwise circumvent requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law. The Tax Act includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on nonexempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the PPACA, effective January 1, 2019, to increase from 50% to 70% 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." In July 2018, CMS published a final rule permitting further collections and payments to and from certain PPACA qualified health plans and health insurance issuers under the PPACA adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In December 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the PPACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the PPACA are invalid as well. On December 18, 2019, a three-judge panel of the U.S. Court of Appeals for the 5th Circuit issued a decision on the appeal of that ruling, holding that the individual mandate is unconstitutional and remanding the case to the Texas District Court Judge to consider certain questions. It is unclear how these decisions, subsequent decisions and appeals, and other efforts to repeal and replace the PPACA will impact the PPACA.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. In August 2011, President Obama signed into law the Budget Control Act of 2011, as amended, which, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which began in 2013 and, following passage of subsequent legislation, including the BBA, will continue through 2027 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was enacted which, among

other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been 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, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal years 2019 and 2020 contains further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The HHS has already started the process of soliciting feedback on some of these measures and is implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs, beginning January 1, 2020. This final rule codified the CMS policy change that was effective January 1, 2019. Although a number of these and other proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. In particular, on September 25, 2019, the Senate Finance Committee introduced the Prescription Drug Pricing Reduction Action of 2019, a bill intended to reduce Medicare and Medicaid prescription drug prices, which would restructure the Medicare Part D benefit, modify payment methodologies for certain drugs, and impose an inflation cap on drug price increases. An even more restrictive bill, the Lower Drug Costs Now Act of 2019, was introduced in the House of Representatives on September 19, 2019, and would require the HHS to directly negotiate drug prices with manufacturers. It is unclear whether either of these bills will make it through both chambers and be signed into law, and if either is enacted, what effect it would have on our business.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs. These measures could reduce future demand for our products or put pressure on our pricing.

Additionally, in May 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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 safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our product candidates. For example, in the EU, we must obtain authorization of a clinical trial application, or CTA, in each member state in which we intend to conduct a clinical trial. Whether or not we obtain FDA approval for a drug, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the drug in those countries. 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.

Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. We are not currently a party to any material legal proceedings, and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results or financial condition.

Facilities

We currently are in a five-year lease for the space for our principal executive offices in New York, New York. We believe that our facilities are adequate to meet our current needs.

Information About Our Executive Officers

The following table sets forth information regarding our executive officers:

Name	Age	Positions(s)
Executive Officers		
Shoshana Shendelman, Ph.D.	41	President, Chief Executive Officer and Chair of the Board of Directors
Riccardo Perfetti, M.D., Ph.D.	60	Chief Medical Officer
Mark J. Vignola, Ph.D.	42	Chief Financial Officer
Adam Hansard	44	Chief Commercial Officer

Shoshana Shendelman, Ph.D. is our founder and has served as our President and Chief Executive Officer and as chair of our board of directors since January 2016. Prior to founding our company, she founded Clearpoint Strategy Group LLC, a boutique life sciences consulting firm, where she served as the Managing Director from July 2012 to December 2016, and served as a Senior Advisor from January 2017 to December 2018. Prior to that, she served as a scientific consultant and analyst at Bridge Scientific Consulting LLC. Dr. Shendelman received her B.S. in biochemistry from Brandeis University and a Ph.D. in Cellular, Molecular and Biophysical Studies (CMBS) from Columbia University Vagelos College of Physicians and Surgeons. We believe that Dr. Shendelman's extensive knowledge of our company as founder, President and Chief Executive Officer and her management background and experience in the healthcare industry qualifies her to serve on our board of directors.

Riccardo Perfetti, M.D., Ph.D. has served as our Chief Medical Officer since August 2018. Prior to joining us, Dr. Perfetti served as a Senior Medical Officer, Vice President and Head of Global Medical Affairs, Diabetes and Cardiovascular Business Unit at Sanofi S.A., a publicly traded pharmaceutical company from October 2007 to September 2018. Prior to joining Sanofi, Dr. Perfetti served in various roles at Amgen Inc., a publicly traded biopharmaceutical company, including as a Director and Global Development Leader in diabetes, obesity, metabolism and endocrinology from December 2004 to August 2007. Dr. Perfetti was previously an associate professor of medicine at University of California in Los Angeles and a professor of medicine at the National Institutes of Health, or NIH. Dr. Perfetti practiced as an endocrinologist at Cedars-Sinai Medical Center and also served as Director of the Diabetes Research Laboratory and Director of the Outpatient Diabetes Program. Dr. Perfetti received his M.D. and Ph.D. in Endocrinology from University La Sapienza in Rome, Italy and received post-graduate training in endocrinology and molecular biology at NIH.

Mark J. Vignola, Ph.D. has served as our Chief Financial Officer since April 2019. Prior to joining the company, from June 2015 to April 2019, he was Executive Director and Head of Corporate Development and Investor Relations at Intercept Pharmaceuticals, a biopharmaceutical company. From July 2011 to May 2015, he was a member of the biotechnology equity research team at Needham and Co. Dr. Vignola received his B.S. in biology from Boston College and a Ph.D. in Molecular Genetics and Microbiology from Duke University.

Adam Hansard has served as our Chief Commercial Officer since March 2020. Prior to joining the company, from March 2019 to February 2020, he was Senior Director of New Product Strategy at Alexion Pharmaceuticals, a biopharmaceutical company. From February 2018 to March 2019, he was Vice President of Business Operations at Syntimmune, a clinical-stage biotech purchased by Alexion in Nov. 2018. From January 2012 to March 2018, Mr. Hansard worked at Sanofi Genzyme, a biotechnology company and wholly-owned subsidiary of Sanofi, a publicly traded, multinational pharmaceutical company, where he served as the North American Senior Director, Chief of Staff of MS Oncology and Immunology and the Senior Director of MS Brand Communications. Mr. Hansard received his Masters in Business Communication from Jones International University and his B.S. in Marketing from the University of West Florida.

Employees

As of December 31, 2019, we had 11 full-time employees, seven of whom were primarily engaged in research and development activities. A total of five employees have an M.D. or Ph.D. degree. None of our employees are represented by a labor union and we consider our employee relations to be good.

Other Information

We were incorporated in Delaware in January 2016 and completed the IPO in May 2019. Our principal executive offices are located at 545 5th Avenue, Suite 1400, New York, New York 10017, and our telephone number is (212) 220-9226.

We maintain a website at www.appliedtherapeutics.com. The contents of our website are not incorporated in, or otherwise to be regarded as part of, this Annual Report on Form 10-K. In this Annual Report on Form 10-K, “Applied Therapeutics,” the “Company,” “we,” “us,” “our” and the “ registrant” refer to Applied Therapeutics, Inc.

Investors and others should note that we announce material financial information to our investors using our investor relations website (http://ir.appliedtherapeutics.com), SEC filings, press releases, public conference calls and webcasts.

ITEM 1A. RISK FACTORS.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks described below, together with other information appearing elsewhere in this Annual Report on Form 10-K, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline and you may lose all or part of your investment.

Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations and the market price of our common stock.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception in January 2016, we have incurred significant operating losses. Our net loss was $45.6 million and $16.5 million for the years ended December 31, 2019 and 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $66.8 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of our product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials. To date, we have never obtained regulatory approval for, or commercialized, any drugs. It could be several years, if ever, before we have a commercialized drug. The net losses we incur may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if, and as, we:

- continue the ongoing and planned development of our product candidates;
- initiate, conduct and complete any ongoing, anticipated or future preclinical studies and clinical trials for our current and future product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any current or future product candidate for which we may obtain marketing approval;
- seek to discover and develop additional product candidates;
- continue to build a portfolio of product candidates through the acquisition or in-license of drugs, product candidates or technologies;
- maintain, protect and expand our intellectual property portfolio;
- meet the requirements and demands of being a public company;
- defend against any product liability claims or other lawsuits related to our products;
- hire additional clinical, regulatory and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

To become and remain profitable, we must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our current and future product candidates, obtaining regulatory approval, procuring commercial-scale manufacturing, marketing and selling any products for which we obtain regulatory approval (including through third parties), as well as discovering or acquiring and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are sufficient to offset our expenses and achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in the initiation and completion of our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our common stock could also cause you to lose all or part of your investment.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company with limited operational history, and our operations to date have been largely focused on raising capital, organizing and staffing our company, identifying and developing our product candidates, and undertaking preclinical and clinical development for our product candidates. As an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization, or arrange for a third party to conduct these activities on our behalf. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Additionally, we expect our financial condition and operating results to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will require substantial additional funding to finance our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate certain of our development programs or other operations.

As of December 31, 2019, our cash, cash equivalents and marketable securities was $38.9 million. In January 2020, we received $134.9 million of net proceeds from the issuance of common stock upon the completion of the Secondary Public Offering, net of underwriting discounts and commissions and estimated offering expenses. Based on our current operating and research and development plans, we believe that our existing cash, cash equivalents, and marketable securities as of December 31, 2019, along with the capital that was raised in January 2020 as part of the Secondary Public Offering will be sufficient to fund our projected operations through at least the next 12 months from the date the financial statements were issued. However, we will need to obtain substantial additional funding in connection with our continuing operations and planned research and clinical development activities. Our future capital requirements will depend on many factors, including:

- the timing, progress and results of our ongoing preclinical studies and clinical trials of our product candidates;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of other product candidates that we may pursue;
- our ability to establish collaborations on favorable terms, if at all;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the cost of any milestone and royalty payments with respect to any approved product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the costs of operating as a public company; and
- the extent to which we acquire or in-license other product candidates and technologies.

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 may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or altogether terminate our research and development programs or future commercialization efforts.

Raising additional capital may cause dilution to our stockholders and restrict our operations or require us to relinquish rights to our product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through public or private equity or debt financings, third party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest in our company may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights.

If we raise additional capital through future collaborations, strategic alliances or third party licensing arrangements, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise

additional capital when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

We have incurred substantial losses since inception and do not expect to become profitable in the near future, if ever. In general, under Section 382 of the United States Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change NOLs to offset future taxable income. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of subsequent changes in our stock ownership (some of which shifts are outside our control). As a result, if, and to the extent that we earn net taxable income, our ability to use our pre-change NOLs to offset such taxable income may be subject to limitations.

For NOLs arising in tax years beginning after December 31, 2017, the Code limits a taxpayer's ability to utilize NOL carryforwards to 80% of taxable income. In addition, NOLs arising in tax years ending after December 31, 2017 can be carried forward indefinitely, but carryback is generally prohibited. NOLs generated in tax years beginning before January 1, 2018 will not be subject to the taxable income limitation, and NOLs generated in tax years ending before January 1, 2018 will continue to have a two-year carryback and 20-year carryforward period. Deferred tax assets for NOLs will need to be measured at the applicable tax rate in effect when the NOL is expected to be utilized. The limitations in the carryforward/carryback periods, as well as the limitation on use of NOLs for NOLs arising in tax years beginning after December 31, 2017 may significantly impact our ability to utilize our NOLs to offset taxable income in the future.

In order to realize the future tax benefits of our NOL carryforwards, we must generate taxable income, of which there is no assurance. Accordingly, we have a full valuation allowance for deferred tax assets as of December 31, 2018 and 2019.

Risks Related to the Development and Commercialization of Our Product Candidates

Our future success is substantially dependent on the successful clinical development, regulatory approval and commercialization of our product candidates. If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates and our ability to generate product revenue will be adversely affected.

We have invested a significant portion of our time and financial resources in the development of AT-001, AT-003 and AT-007. Our business is dependent on our ability to successfully complete development of, obtain regulatory approval for, and, if approved, successfully commercialize our product candidates in a timely manner. We may face unforeseen challenges in our drug development strategy, and we can provide no assurances that our drug design will prove to be effective, that we will be able to take advantage of expedited regulatory pathways for any of our product candidates, or that we will ultimately be successful in our future clinical trials.

We have not obtained regulatory approval for any product candidate, and it is possible that any product candidates we may seek to develop in the future will not obtain regulatory approval. Neither we nor any future collaborator is permitted to market any product candidates in the United States or abroad until we receive regulatory approval from the FDA or applicable foreign regulatory agency. The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign regulatory authorities is unpredictable and typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, 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.

Prior to obtaining approval to commercialize any product candidate in the United States or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidate is safe and effective for its intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe that the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program, requiring their alteration.

Of the large number of products in development, only a small percentage successfully complete the FDA or comparable foreign regulatory authorities approval processes and are commercialized. The lengthy approval or marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval or marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we eventually complete clinical testing and receive approval of a new drug application, or NDA, or foreign marketing application for our product candidates, the FDA or the comparable foreign regulatory authorities may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-market clinical trials. The FDA or the comparable foreign regulatory authorities also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA or comparable foreign regulatory authorities may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would adversely impact our business and prospects.

In addition, the FDA or comparable foreign regulatory authorities may change their policies, adopt additional regulations or revise existing regulations or take other actions, which may prevent or delay approval of our future product candidates under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained.

Furthermore, even if we obtain regulatory approval for our product candidates, we will still need to develop a commercial organization, establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third party and government payors, including government health administration authorities. If we are unable to successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business.

The development of additional product candidates is risky and uncertain, and we can provide no assurances that we will be able to replicate our approach to drug development for other disease indications.

Efforts to identify, acquire or in-license, and then develop, product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our efforts may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development, approved products or commercial revenues for many reasons, including the following:

- the methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render any product candidates we develop obsolete;
- any product candidates we develop may be covered by third parties' patents or other exclusive rights;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;

- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and

- a product candidate may not be accepted as safe and effective by physicians, patients, the medical community or third party payors.

We have limited financial and management resources and, as a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater market potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. 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 circumstances under which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. In addition, we may not be successful in replicating our approach to drug development for other disease indications. If we are unsuccessful in identifying and developing additional product candidates or are unable to do so, our business may be harmed.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and we cannot assure you that any ongoing, planned or future clinical trials will lead to results sufficient for the necessary regulatory approvals.

Success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical studies and Phase 1 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical studies and earlier clinical trials does not ensure that later efficacy trials will be successful, nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through earlier clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

Clinical drug development involves a lengthy and expensive process. We may incur additional costs and encounter substantial delays or difficulties in our clinical trials.

We may not commercialize, market, promote or sell any product candidate without obtaining marketing approval from the FDA or other comparable regulatory authority, and we may never receive such approvals. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome. For example, we intend to conduct an additional Phase 1 clinical trial of AT-007 for the treatment of galactosemia in a pediatric population upon successful completion of the Phase 1 clinical trial in adults. Successful completion of the trial in adults may take longer than we expect, and the FDA may express additional concerns or require additional trials in adults, which may delay our clinical development plans for AT-007.

A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events prior to, during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including the following:

- delays in reaching a consensus with regulatory authorities on the design or implementation of our clinical trials;
- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post-treatment follow-up or we may fail to recruit suitable patients to participate in a trial;
- clinical trials of our product candidates may produce negative or inconclusive results;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future drug sales or other sources. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring competing drugs to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval, or not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;

- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including in the form of a risk evaluation and mitigation strategy, or REMS;
- be subject to additional post-marketing testing requirements;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all.

Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's current Good Clinical Practice, or GCP, regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our investigational new drug applications, or INDs, or the conduct of these trials. Therefore, we cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be negatively impacted, and our ability to generate revenues from our product candidates may be delayed.

All of our current product candidates that have proceeded to clinical trials target inhibition of aldose reductase. There can be no assurance that aldose reductase inhibitors will ever receive regulatory approval.

All of our current product candidates that have proceeded to clinical trials target inhibition of the aldose reductase enzyme. There are no currently approved aldose reductase inhibitors on the market outside of Japan, India and China, and there can be no assurance that aldose reductase inhibitors will ever receive regulatory approval in all other countries, including the United States. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. Our current product candidates, including AT-001, AT-003 and AT-007, may face similar or different challenges that prevent their successful commercialization.

We may not be able to obtain or maintain rare pediatric disease designation or exclusivity for our product candidates, which could limit the potential profitability of our product candidates.

We have obtained orphan drug designation, and we may seek rare pediatric disease designation, from the FDA for AT-007 for the treatment of galactosemia. The FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is defined as a disease or condition that either affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

For the purposes of the rare pediatric disease program, a “rare pediatric disease” is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years or a rare disease or conditions within the meaning of the Orphan Drug Act. Under the FDA’s rare pediatric disease priority review voucher, or RPD-PRV, program, upon the approval of an NDA for the treatment of a rare pediatric disease, the sponsor of such application would be eligible for an RPD-PRV that can be used to obtain priority review for a subsequent NDA. The sponsor of the application may transfer (including by sale) the RPD-PRV to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. Congress has extended the RPD-PRV program until September 30, 2020, with potential for vouchers to be granted until 2022. This program has been subject to criticism, including by the FDA. As such, it is possible that even if we obtain approval for AT-007 for the treatment of galactosemia and qualify for a RPD-PRV, the program may no longer be in effect at the time of approval. Also, although priority review vouchers may be sold or transferred to third parties, there is no guaranty that we will be able to realize any value if we obtained, and subsequently were able to sell, a priority review voucher.

A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened.

We may seek fast track designation from the FDA for AT-001 for DbCM. Even if granted, fast track designation may not actually lead to a faster development, regulatory review or approval process.

If a product candidate is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet needs for this condition, the sponsor may apply for FDA fast track designation. If fast track designation is obtained, the FDA may prioritize interactions with the sponsor concerning the designated development program and initiate review of sections of an NDA before the application is complete, known as “rolling review.” Fast track designation would not ensure that we would experience a faster development, regulatory review or approval process compared to conventional FDA procedures or that we would ultimately obtain regulatory approval. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

We intend to seek approval from the FDA through the use of accelerated registration pathways. If we are unable to obtain approval under an accelerated pathway, we may be required to conduct additional preclinical studies or clinical trials, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approvals. Even if we receive approval from the FDA to utilize an

accelerated registration pathway, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We intend to seek an accelerated approval development pathway for our product candidates. Under the accelerated approval provisions of the Federal Food, Drug, and Cosmetic Act, or the FDCA, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product designed to treat a serious or life-threatening condition that provides meaningful therapeutic advantage over available therapies and demonstrates an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval development pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical profile or risks and benefits for accelerated approval. The FDA may require that any such confirmatory studies be initiated or substantially underway prior to the submission of an application for accelerated approval. If such post-approval studies fail to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug. Because we are still in early stages of our clinical trials, we can provide no assurances that our biomarker-based approach will be successful in demonstrating a causal link to the relevant outcomes we are evaluating. If our approach is not successful, we may be required to conduct longer clinical trials.

If we choose to pursue accelerated approval, we intend to seek feedback from the FDA or will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that, after our evaluation of the feedback from the FDA or other factors, we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Furthermore, even if we submit an application for accelerated approval, there can be no assurance that the application will be accepted or that approval will be granted on a timely basis, or at all. The FDA also could require us to conduct further studies or trials prior to considering our application or granting approval of any type. We might not be able to fulfill the FDA's requirements in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA. A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate would result in a longer time period to commercialize such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we receive accelerated approval from the FDA, we will be subject to rigorous post-marketing requirements, including the completion of confirmatory post-market clinical trial(s) to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw accelerated approval for multiple reasons, including if we fail to conduct any required post-market study with due diligence, a post-market study does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false or misleading.

A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate that we may choose to develop would result in a longer time period prior to commercializing such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be delayed, made more difficult or rendered impossible by multiple factors outside our control.

Identifying and qualifying patients to participate in our clinical trials is critical to our success. We may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development and approval

of our product candidates. Even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data, the number and nature of competing treatments and ongoing clinical trials of competing therapies for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the trial. Because our focus includes rare disorders, there are limited patient pools from which to draw in order to complete our clinical trials in a timely and cost-effective manner. Accordingly, enrollment of our clinical trials could take significantly longer than projected, which would delay any potential approval of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

For example, upon successful completion of the planned Phase 1 clinical trial in adults, we intend to conduct an additional Phase 1 clinical trial of AT-007 for the treatment of galactosemia in a pediatric population. We are doing this in order to obtain data on patients representing the most vulnerable subset of our intended population. Such pediatric patients may be difficult to enroll in this trial, and the lack of data on these patients may negatively impact the approvability or labeling of galactosemia.

Our efforts to build relationships with patient communities may not succeed, which could result in delays in patient enrollment in our clinical trials. Any negative results we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates or could render further development impossible. In addition, we may rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to ensure their actual performance.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur.

In addition, it is possible that as we test our product candidates in larger, longer and more extensive clinical trials, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects or patients. Many times, side effects are only detectable after investigational drugs are tested in large-scale pivotal trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates have side effects or cause serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition.

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

From time to time, we may publish interim, "top-line" or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until

the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we believe they are or any approval we obtain is based on a narrower definition of the patient population, our business may suffer.

We currently focus our drug development on product candidates for the treatment of diseases with high unmet medical need. Our eligible patient population and pricing estimates may differ significantly from the actual market addressable by our product candidates. Our estimates of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and analyses. These estimates have been derived from a variety of sources, including the scientific literature, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of the diseases we are targeting. The number of patients may turn out to be lower than expected. Likewise, the potentially addressable patient population for each of our product candidates may be limited or may not be receptive to treatment with our product candidates, and new patients may become increasingly difficult to identify or access. If the market opportunities for our product candidates are smaller than we estimate, we may not be able to achieve our forecast revenue, which could hinder our business plan and adversely affect our business and results of operations.

We face substantial competition, which may result in others developing or commercializing drugs before or more successfully than us.

The development and commercialization of new drugs is highly competitive. We may face potential competition with respect to our current product candidates and may face competition with respect to any other product candidates that we may seek to develop or commercialize in the future from pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research institutions.

Our competitors may have an advantage over us due to their greater size, resources and institutional experience. In particular, these companies have greater experience and expertise in securing reimbursement, government contracts and relationships with key opinion leaders, conducting testing and clinical trials, obtaining and maintaining regulatory approvals and distribution relationships to market products and marketing approved drugs. These companies also have significantly greater research and marketing capabilities than we do. If we are not able to compete effectively against existing and potential competitors, our business and financial condition may be harmed.

As a result of these factors, our competitors may obtain regulatory approval of their drugs before we are able to, which may limit our ability to develop or commercialize our product candidates. Our competitors may also develop therapies that are safer, more effective, more widely accepted or less expensive than ours, and may also be more successful than we are in manufacturing and marketing their drugs. These advantages could render our product candidates obsolete or non-competitive before we can recover the costs of such product candidates' development and commercialization.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties 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.

We may explore strategic collaborations that may never materialize or we may be required to relinquish important rights to and control over the development and commercialization of our product candidates to any future collaborators.

Over time, our business strategy includes acquiring or in-licensing additional product candidates for treatments of diseases with high unmet medical need. As a result, we intend to periodically explore a variety of possible strategic collaborations in an effort to gain access to additional product candidates or resources. These strategic collaborations may include partnerships with large strategic partners, particularly for the development of DPN treatments using AT-001. At the current time however, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic collaborations because of the numerous risks and uncertainties associated with establishing them.

Future collaborations could subject us to a number of risks, including:

- we may be required to undertake the expenditure of substantial operational, financial and management resources;
- we may be required to issue equity securities that would dilute our stockholders' percentage ownership of our company;
- we may be required to assume substantial actual or contingent liabilities;
- we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our product candidates;
- strategic collaborators may select indications or design clinical trials in a way that may be less successful than if we were doing so;
- strategic collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic collaborators may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs;
- strategic collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products;
- disputes may arise between us and our strategic collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic collaborators may experience financial difficulties;
- strategic collaborators may not properly maintain, enforce or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a strategic collaborator's business strategy may adversely affect a strategic collaborator's willingness or ability to complete its obligations under any arrangement;

- strategic collaborators could decide to move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors; and

- strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our product candidates.

Even if any product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third party payors or others in the medical community necessary for commercial success.

Even if any product candidates receive marketing approval, they may fail to gain market acceptance by physicians, patients, third party payors and others in the medical community. If such product candidates do not achieve an adequate level of acceptance, we may not generate significant drug revenue and may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the convenience and ease of administration compared to alternative treatments and therapies;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

- the efficacy and potential advantages compared to alternative treatments and therapies;

- the effectiveness of sales and marketing efforts;

- the strength of our relationships with patient communities;

- the cost of treatment in relation to alternative treatments and therapies, including any similar generic treatments;

- our ability to offer such drug for sale at competitive prices;

- the strength of marketing and distribution support;

- the availability of third party coverage and adequate reimbursement;

- the prevalence and severity of any side effects; and

- any restrictions on the use of the drug together with other medications.

Our efforts to educate physicians, patients, third party payors and others in the medical community on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our product candidates. Because we expect sales of our product candidates, if approved, to generate substantially all of our revenues for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business.

Even if we obtain regulatory approvals for our product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain regulatory approvals for our product candidates, such approvals will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates may also be subject to a REMS, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing,

including Phase 4 trials, and surveillance to monitor the quality, safety and efficacy of the drug. Such regulatory requirements may differ from country to country depending on where we have received regulatory approval.

In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of our product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or comparable foreign marketing application or any supplements thereto submitted by us or our partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and harm our business, financial condition, results of operations and prospects.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are not able to maintain regulatory compliance with the Cures Act, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

In addition, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain

policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict how these executive actions, including the executive orders, will be implemented and the extent to which they will affect the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing them, if and when they are approved.

To successfully commercialize any product candidate that may result from our development programs, we will need to build out our sales and marketing capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any product candidate we may develop will be expensive and time-consuming and could delay any drug launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may seek to enter into collaborations with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our product candidates, or we are unable to develop the necessary capabilities on our own, we may be unable to generate sufficient revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We will likely also face competition if we seek third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval outside the United States, which would limit our market opportunities.

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable foreign regulatory authorities also must approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for any product candidates, if approved, is also subject to approval. Obtaining approval for our product candidates in the European Union from the European Commission following the opinion of the European Medicines Agency, or the EMA, if we choose to submit a marketing authorization application there, would be a lengthy and expensive process. Even if a product candidate is approved, the EMA may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. 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 product candidates in certain countries.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for our product candidates may be withdrawn. If we fail to comply with the applicable regulatory requirements, 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, financial condition, results of operations and prospects could be harmed.

If we commercialize our product candidates outside the United States, a variety of risks associated with international operations could harm our business.

We intend to seek approval to market our product candidates outside the United States, and may do so for future product candidates. If we market approved products outside the United States, we expect that we will be subject to additional risks in commercialization, including:

- different regulatory requirements for approval of therapies in foreign countries;
- reduced protection for intellectual property rights;
- 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 reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- 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.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by many of the individual countries in which we may operate, with which we will need to comply. Many biopharmaceutical companies have found the process of marketing their products in foreign countries to be challenging.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk if we commercialize any product candidate that we may develop. If we cannot successfully defend ourselves against claims that any such product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidate that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;

- increased insurance costs;
- the inability to commercialize any product candidate that we may develop; and
- injury to our reputation and significant negative media attention.

Any such outcomes could negatively impact our business, financial condition, results of operations and prospects.

Our insurance policies may be inadequate and potentially expose us to unrecoverable risks.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance availability, coverage terms and pricing continue to vary with market conditions. We endeavor to obtain appropriate insurance coverage for insurable risks that we identify; however, we may fail to correctly anticipate or quantify insurable risks, we may not be able to obtain appropriate insurance coverage and insurers may not respond as we intend to cover insurable events that may occur. We have observed rapidly changing conditions in the insurance markets relating to nearly all areas of traditional corporate insurance. Such conditions have resulted in higher premium costs, higher policy deductibles, and lower coverage limits. For some risks, we may not have or maintain insurance coverage because of cost or availability.

Risks Related to Regulatory Compliance

Our relationships with customers, physicians, and third party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, physicians and third party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations. For additional information on the healthcare laws and regulations that we may be subject to, see “Business — Government Regulation and Product Approval.”

Ensuring that our business arrangements with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving 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 governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations.

If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development,

manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have an adverse effect on our ability to compete in the marketplace.

Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell profitably, if approved.

Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third party payors, including government health administration authorities, managed care organizations and other private health insurers. Third party payors decide which therapies they will pay for and establish reimbursement levels. While no uniform policy for coverage and reimbursement exists in the United States, third party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. Therefore, one payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether or not it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a payor's list of covered drugs, or formulary, generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our product candidates, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

Third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates that we develop.

Healthcare reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes, as well as judicial challenges, regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

Further, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the PPACA, was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the United States. Some of the provisions of the PPACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges, as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. For

example, the Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called "Cadillac" tax on certain high-cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amended the PPACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS published a final rule permitting further collections and payments to and from certain PPACA-qualified health plans and health insurance issuers under the PPACA adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the PPACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the PPACA are invalid as well. On December 18, 2019, a three-judge panel of the U.S. Court of Appeals for the 5th Circuit issued a decision on the appeal of that ruling, holding that the individual mandate is unconstitutional and remanding the case to the Texas District Court Judge to consider certain questions. It is unclear how these decisions, subsequent decisions and appeals, and other efforts to repeal and replace the PPACA will impact the PPACA. Congress may consider additional legislation to repeal or repeal and replace other elements of the PPACA. We continue to evaluate the effect that the PPACA and its possible repeal and replacement may have on our business and the potential profitability of our product candidates.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the BBA, which will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, which will be fully operational in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

Further, in the United States there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. While some of the proposed measures will require authorization through additional legislation to become effective, the U.S. Congress and the Trump administration have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. On September 25, 2019, the Senate Finance Committee introduced the Prescription Drug Pricing Reduction Act of 2019, a bill intended to reduce Medicare and Medicaid prescription drug prices, which would restructure the Medicare Part D benefit, modify payment methodologies for certain drugs and impose an inflation cap on drug price increases. An even more restrictive bill, the Lower Drug Costs Now Act of 2019, was introduced in the House of Representatives on September 19, 2019, and would require the U.S. Department of Health and Human Services (HHS) to directly negotiate drug prices with manufacturers. It is unclear whether either of these bills will make it through both chambers and be signed into law, and, if either is enacted, what effect it would have on our business. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our current or any future product candidates or additional pricing pressures. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing or new requirements or policies, or if we or such third parties

are not able to maintain regulatory compliance, our current or any future product candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on demand for our product candidates if they are approved. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates. For additional information on healthcare reform, see "Business — Government Regulation and Product Approval."

Risks Related to Our Dependence on Third Parties

We intend to rely on third parties to produce clinical and commercial supplies of our product candidates.

We do not own or operate facilities for drug manufacturing, storage and distribution, or testing. We are dependent on third parties to manufacture the clinical supplies of our current and any future product candidates. 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 to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP requirements, for manufacture of both active drug substance and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA 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 regulatory approval for or market our product candidates, if approved. Any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates.

We also intend to rely on third party manufacturers to supply us with sufficient quantities of our product candidates to be used, if approved, for commercialization. We do not yet have a commercial supply agreement for commercial quantities of drug substance or drug product. If we are not able to meet market demand for any approved product, it would negatively impact our ability to generate revenue, harm our reputation, and could have an adverse effect on our business and financial condition.

Further, our reliance on third party manufacturers entails risks to which we would not be subject if we manufactured product candidates ourselves, including:

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- issues related to scale-up of manufacturing;

- costs and validation of new equipment and facilities required for scale-up;
- our third party manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our third party manufacturers may fail to comply with cGMP requirements and other inspections by the FDA or other comparable regulatory authorities;
- our inability to negotiate manufacturing agreements with third parties under commercially reasonable terms, if at all;
- breach, 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 single sources for drug components;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single-source supplier;
- our third party manufacturers may not devote sufficient resources to our product candidates;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third party manufacturers in the manufacturing process for 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; and
- carrier disruptions or increased costs that are beyond our control.

In addition, if we enter into a strategic collaboration with a third party for the commercialization of our current or any future product candidates, we will not be able to control the amount of time or resources that they devote to such efforts. If any strategic collaborator does not commit adequate resources to the marketing and distribution of our product candidates, it could limit our potential revenues.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize our current or any future product candidates once approved. Some of these events could be the basis for FDA action, including injunction, request for recall, seizure, or total or partial suspension of production.

Our business involves the use of hazardous materials and we and our third party manufacturers and suppliers must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do, or interrupt our, business.

Our research and development activities and our third party manufacturers' and suppliers' activities involve the generation, storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds and wastes. We and our manufacturers and suppliers are subject to environmental, health and safety laws and regulations governing, among other matters, the use, manufacture, generation, storage, handling, transportation, discharge and disposal of these hazardous materials and wastes and worker health and safety. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination or injury, which could result in an interruption of our commercialization efforts, research and development efforts and business operations, damages and significant cleanup costs and liabilities under applicable environmental, health and safety laws and regulations. We also cannot guarantee that the safety procedures utilized by our third party manufacturers for handling and disposing of these

materials and wastes generally comply with the standards prescribed by these laws and regulations. We may be held liable for any resulting damages, costs or liabilities, which could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental, health and safety laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Failure to comply with these environmental, health and safety laws and regulations may result in substantial fines, penalties or other sanctions. We do not currently carry environmental insurance coverage.

We rely on third parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We do not currently have the ability to independently conduct any clinical trials. We intend to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our preclinical studies and clinical trials, and we expect to have limited influence over their actual performance. We rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future preclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our preclinical studies and clinical trials 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 and our CROs are required to comply with the good laboratory practices, or GLPs, and GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. The regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we rely on CROs to conduct GCP-compliant clinical trials, we remain responsible for ensuring that each of our GLP preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations. If we or our CROs fail to comply with GCPs, 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. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process.

Our reliance on third parties to conduct clinical trials will result in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with CROs and other third parties can be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Such parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience regulatory compliance issues; or
- undergo changes in priorities or become financially distressed.

These factors may adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or fail to comply with regulatory requirements, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed. While we will have agreements governing their activities, our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and preclinical programs. These CROs 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 which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology.

If our relationship with any of these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires 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 negatively impact our ability to meet our desired clinical development timelines. While we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, financial condition and prospects.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of our product candidates.

Risks Related to Our Intellectual Property

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. If we breach our license agreements with Columbia University or any of the other agreements under which we acquired, or will acquire, the intellectual property rights to our product candidates, we could lose the ability to continue the development and commercialization of the related product.

The licensing of intellectual property is of critical importance to our business and to our current and future product candidates, and we expect to enter into additional such agreements in the future. In particular, our current product candidates AT-001, AT-003 and AT-007 are dependent on our license agreement with The Trustees of Columbia University in the City of New York, or Columbia University. Pursuant to that license agreement with Columbia University, or the 2016 Columbia Agreement, Columbia University granted us an exclusive license under two important patent families, and a nonexclusive license to certain know-how, owned by Columbia University to develop, manufacture or commercialize certain compounds, including AT-001, AT-003 and AT-007, for the diagnosis and treatment of human and animal diseases and conditions. The license grant is worldwide, with the exception of the patent family that covers AT-001 and AT-003. The license grant for the patent family that covers AT-001 and AT-003 excludes patent rights in China, Taiwan, Hong Kong and Macao, which Columbia University has exclusively licensed to a third party. We cannot prevent Columbia University's third party licensee from developing, manufacturing or commercializing certain compounds, including AT-001 and AT-003, but not including AT-007, in China, Taiwan, Hong Kong and Macao, and we cannot develop, manufacture or commercialize AT-001 or AT-003 in these territories, which could have a negative effect on our business. In addition, we entered into the 2019 Columbia Agreement, the 2019 Research Agreement and the PI3k Columbia Research Agreement, whereby, among other things, Columbia University granted to us an exclusive license under certain patents, and a non-exclusive license to certain know-how, in each case to develop, manufacture and commercialize certain PI3K inhibitor products, including AT-104.

We do not have the right to control the preparation, filing, prosecution and maintenance of patents and patent applications covering the technology that we license under either of the Columbia Agreements. Therefore, we cannot always be certain that these patents and patent applications will be prepared, filed, prosecuted and maintained in a manner consistent with the best interests of our business. Although we have a right to have our comments considered in connection with the prosecution process, if Columbia University fails to prosecute and maintain such patents, or loses rights to those patents or patent applications as a result of its control of the prosecution activities, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected.

If we fail to meet our obligations under either Columbia Agreement in any material respect and fail to cure such breach in a timely fashion, then Columbia University may terminate such Columbia Agreement. If either Columbia Agreement is terminated, and we lose our intellectual property rights under such Columbia Agreement, this may result in complete termination of our product development and any commercialization efforts for the product candidates that are subject to such agreement, including AT-001, AT-003, AT-007 and AT-104. While we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by us, and otherwise seek to preserve our rights under each Columbia Agreement, we may not be able to do so in a timely manner, at an acceptable cost or at all. For more information on the Columbia Agreement, see the section titled "Business — Exclusive License Agreement with Columbia University" and "Certain Relationships and Related Party Transactions — Columbia University License Agreements."

Furthermore, license agreements we enter into in the future may not provide exclusive rights to use intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses.

If we are unable to obtain and maintain patent protection for our product candidates and technology, or if the scope of the patent protection obtained is not sufficiently broad or robust, our competitors could develop and commercialize products and technology similar or identical to ours, and our ability to successfully commercialize our product candidates and technology may be adversely affected.

Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates and our technology. We and our licensors have sought, and intend to seek, to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates and our technology that are important to our business.

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 patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by such third party, or by the U.S. Patent and Trademark Office, or USPTO, itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

We or our licensors have not pursued or maintained, and may not pursue or maintain in the future, patent protection for our product candidates in every country or territory in which we may sell our products, if approved. 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 may not be able to prevent third parties from infringing our patents in all countries outside the United States, or from selling or importing products that infringe our patents in and into the United States or other jurisdictions.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if the patent applications we license or own do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third

parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for noncommercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

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

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. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or patent applications will have to be paid to the USPTO and various government patent agencies outside the United States over the lifetime of our owned and licensed patents and/or applications and any patent rights we may own or license in the future. We rely on our service providers or our licensors to pay these fees. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, nonpayment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products that are the same as or similar to our product candidates, which would have an adverse effect on our business. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, 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. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

In addition, if we fail to apply for applicable patent term extensions or adjustments, we will have a more limited time during which we can enforce our granted patent rights. In addition, if we are responsible for patent prosecution and maintenance of patent rights in-licensed to us, any of the foregoing could expose us to liability to the applicable patent owner.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of product candidates such as AT-001, AT-003 and AT-007, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we have or will obtain patent rights. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent; *provided* that the patent is not enforceable for more than 14 years from the date of drug approval, which is limited to the approved indication (or any additional indications approved during the period of extension). Furthermore, only one patent per approved product can be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may 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 be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of others with whom we may collaborate to develop, manufacture, market and sell our current and any future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and any future product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this is a high burden and requires us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Other companies and research institutions have filed, and may file in the future, patent applications related to AR inhibitors and their therapeutic use. Some of these patent applications have already been allowed or issued, and others may issue in the future. While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third party patents or patent applications, or we may incorrectly conclude that a third party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that our product candidate infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from nonpracticing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit.

If we are found to infringe a third party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third party to continue developing, manufacturing and marketing our product candidate(s) and technology. Under any such license, we would most likely be required to pay various types of fees, milestones, royalties or other amounts. Moreover, we may not be able to obtain any required license on commercially reasonable terms or at all.

The licensing or acquisition of third party intellectual property rights is a competitive area, and more established companies may also pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have an adverse effect on our business, financial condition, results of operations and prospects. Furthermore, even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidate. 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 or other intellectual property right. We may be required to indemnify collaborators or contractors against such claims. A finding of infringement could prevent us from manufacturing and commercializing our current or any future product candidates or force us to cease some or all of our business operations, which could harm our business. Even if we are successful in defending against such claims, litigation can be expensive and time-consuming and would divert management's attention from our core business. 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 an adverse effect on the price of our common stock.

Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be

forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

We may be involved in lawsuits to protect or enforce our patents, the patents of our licensors or our other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe, misappropriate or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming and are likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our owned or licensed patents at risk of being invalidated or interpreted narrowly and could put our owned or licensed patent applications at risk of not issuing. The initiation of a claim against a third party might also cause the third party to bring counterclaims against us, such as claims asserting that our patent rights are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review, post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is or will be no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license, or if the license offered as a result is not on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

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 an adverse effect on the price of our common stock.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our current and any future product candidates.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued

patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. The America Invents Act also includes a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, inter partes review, and derivation proceedings. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we own, have licensed or might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we own or have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents covering our current and any future product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we or our licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents, and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so 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, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to

any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Since we rely on third parties to help us discover, develop and manufacture our current and any future product candidates, or if we collaborate with third parties for the development, manufacturing or commercialization of our current or any future product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third party illegally or unlawfully obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into nondisclosure 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. We also enter into confidentiality and invention or patent assignment agreements with our employees, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any 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 inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all of the competitive advantages we derive

from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our data and other confidential information by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and detecting the disclosure or misappropriation of confidential information and enforcing a claim that a party illegally disclosed or misappropriated confidential information is difficult, expensive and time-consuming, and the outcome is unpredictable. Further, we may not be able to obtain adequate remedies for any breach. In addition, our confidential information may otherwise become known or be independently discovered by competitors, in which case we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. We have not yet selected trademarks for our product candidates and have not yet begun the process of applying to register trademarks for our current or any future product candidates. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with our current or any other product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

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

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business. The following examples are illustrative:

- others may be able to make compounds or formulations that are similar to our product candidates but that are not covered by the claims of any patents, should they issue, that we own or license;
- we or our licensors might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or license;
- we or our licensors might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;

- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;

- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable; and

- the patents of others may have an adverse effect on our business.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

We are highly dependent on the services of our Chief Executive Officer and Chairman, Dr. Shoshana Shendelman, and our Chief Medical Officer, Dr. Riccardo Perfetti, and if we are not able to retain these members of our management team or recruit and retain additional management, clinical and scientific personnel, our business will be harmed.

We are highly dependent on our Chief Executive Officer and Chairman, Dr. Shoshana Shendelman, and our Chief Medical Officer, Dr. Riccardo Perfetti. Each of them may currently terminate their employment with us at any time. The loss of the services of either of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining other senior executives, qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high-quality personnel, our ability to pursue our growth strategy will be limited.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. Additionally, we do not currently maintain “key person” life insurance on the lives of our executives or any of our employees.

We expect to expand our organization, and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2019, we had 11 full-time employees. As the clinical development of our product candidates progresses, we also expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product

candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a significant disruption of our product development programs and our ability to operate our business effectively, and adversely affect our business and operating results.

Our internal computer systems, cloud-based computing services and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage or interruption from computer viruses, data corruption, cyber-based attacks, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, federal, state and international laws and regulations, such as the European Union's General Data Protection Regulation, or the GDPR, which took effect in May 2018, can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties and significant legal liability, if our information technology security efforts fail. In addition, our software systems include cloud-based applications that are hosted by third party service providers with security and information technology systems subject to similar risks. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these 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 result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects.

Any future acquisitions or strategic collaborations may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and/or subject us to other risks.

From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent or unknown liabilities;
- assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we engage in future acquisitions or strategic partnerships, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses, and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or drugs that may be important to the development of our business.

Our business may be adversely affected by the recent coronavirus outbreak.

In December 2019, a novel strain of coronavirus, referred to as 2019-ncov, Covid-19 coronavirus epidemic, or Covid-19, was reported to have surfaced in Wuhan, China. Covid-19 has since spread to other regions in China and other countries, including jurisdictions, such as the EU, in which we have partnered with CROs to conduct clinical studies. There is a possibility that such CROs may become unavailable or that the clinical trials they manage may be delayed due to Covid-19 or containment efforts associated with it. Such events may lead to termination of our relationship with affected CROs, effecting the development and study of our product candidates.

More recently, Covid-19 has spread to the United States where we have our executive offices and principal operations. Infections and deaths related to Covid-19 may disrupt the United States' healthcare and healthcare regulatory systems. Such disruptions could divert healthcare resources away from, or materially delay FDA approval with respect to, our clinical trials. It is unknown how long these disruptions could continue, were they to occur. In addition, other known and unknown factors caused by Covid-19 could materially delay our clinical trials, 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. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

In addition, we have in the past and may in the future source equipment and materials from China and other countries affected by Covid-19. If we were to engage with third party manufacturers in such countries in the future, there would be an increased risk of supply interruption, resulting in business/operational disruption.

Covid-19's spread, which has caused a broad impact globally, such as restrictions on travel and quarantine policies put into place by businesses and governments, may materially affect us economically. While the potential economic impact brought by and the duration of Covid-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of Covid-19 could materially affect our business and the value of our common stock.

While it is too early to tell whether Covid-19 will have a material effect on our business over time, we continue to monitor the situation as it unfolds. The extent to which Covid-19 impacts our results will depend on many factors and future developments, including new information about Covid-19 and any new government regulations which may emerge to contain the virus, among others.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.

The market price of our common stock is likely to be volatile. The stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the offering price. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report on Form 10-K, the market price for our common stock may be influenced by the following:

- the commencement, enrollment or results of our planned or future clinical trials of our product candidates or those of our competitors;
- the success of competitive drugs or therapies;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;
- 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 our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;

- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States and abroad; and
- investors' general perception of us and our business.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our common stock.

Some companies that have experienced volatility in the trading price of their shares have been the subject of securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common stock.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Based upon shares of our common stock outstanding as of December 31, 2019, our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock, in the aggregate, beneficially own shares representing approximately 47% of our outstanding common stock. If our executive officers, directors and stockholders who owned more than 5% of our outstanding common stock acted together, they may be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. The concentration of voting power and transfer restrictions could delay or prevent an acquisition of our company on terms that other stockholders may desire or result in the management of our company in ways with which other stockholders disagree.

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

The trading market for our common stock will be influenced by the research and reports that industry or financial analysts publish about us or our business. Equity research analysts may discontinue research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research about us. If one or more equity research analysts cease coverage of us or fail to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common stock to decline.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

You should not rely on an investment in our common stock to provide dividend income. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

We have broad discretion in the use of our cash and cash equivalents and may use them ineffectively, in ways with which you do not agree or in ways that do not increase the value of your investment.

Our management will have broad discretion in the application of our cash and cash equivalents and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in additional operating losses that could have a negative impact on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

Future sales of common stock by holders of our common stock, or the perception that such sales may occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2019, we had outstanding 18,531,560 shares of common stock. A substantial number of such shares are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold in the future.

We further have registered all shares of common stock that we may issue in the future or have issued to date under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and certain lock-up agreements. Sales of a large number of the shares issued under these plans in the public market could have an adverse effect on the market price of our common stock.

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

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not EGCs, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and

- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict whether investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile. We currently take advantage of some or all of these reporting exemptions until we are no longer an EGC. We will remain an EGC until the earlier of (i) December 31, 2024, (ii) the last day of the fiscal year in which we have total annual gross revenue of at least $1.07 billion, (iii) the last day of the first fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (iv) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

In addition, under Section 107(b) of the JOBS Act, EGCs can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not EGCs.

We have incurred increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, and particularly after we are no longer an EGC, we incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the Securities and Exchange Commission (the “SEC”), and The Nasdaq Stock Market LLC have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to comply with these requirements. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these

provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called "poison pill," that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least $66^{2}/_{3}\%$ of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the 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, with respect to any state actions or proceedings under Delaware statutory or common law, the Court of Chancery of the State of Delaware is 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 or any of our directors, officers, employees or agents arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws;
- any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; and

- any action asserting a claim against us or any of our directors, officers, employees or agents that is governed by the internal-affairs doctrine.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable 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 an exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could harm our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 2. PROPERTIES.

Our corporate headquarters are located at 545 Fifth Ave, Suite 1400, New York, NY 10017 where we lease office space pursuant to a lease agreement that commenced on October 31, 2019 and expires on October 31, 2024. We believe that our existing facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

ITEM 3. LEGAL PROCEEDINGS.

We are not a party to any legal proceedings, and we are not aware of any claims or actions pending or threatened against us. In the future, we might from time to time become involved in litigation relating to claims arising from our ordinary course of business, the resolution of which we do not anticipate would have a material adverse impact on our financial position, results of operations or cash flows.

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

On May 16, 2019, our common stock began trading on the Nasdaq Global Market under the symbol "APLT." Prior to that time, there was no public market for our common stock.

Stockholders

As of December 31, 2019, there were 125 stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street names by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future

earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

Equity Compensation Plans

The information required by Item 5 of Form 10-K regarding equity compensation plans is incorporated herein by reference to Item 11 of Part III of this Annual Report.

Recent Sales of Unregistered Securities

The following list sets forth information as to all securities we have sold between December 31, 2016 and December 31, 2019:

(1) We granted options to purchase an aggregate of 2,679,820 shares of common stock, with exercise prices ranging from $0.04 to $4.70 per share, to certain of our employees, directors and consultants pursuant to our 2016 Equity Incentive Plan, as amended, or the 2016 Plan. Of these options, options to purchase 55,081 shares have been exercised for cash consideration in the aggregate amount of $46,287.92, and options to purchase 2,624,738 shares of common stock remain outstanding.

(2) In February 2017, we issued 486,077 shares of common stock to the Trustees of Columbia University in the City of New York, or Columbia University, as partial consideration of Columbia University's execution and delivery to us of that certain license agreement, representing a fair value of $0.5 million.

(3) Between January and March 2017, we issued and sold an aggregate of 3,093,898 shares of our Series A convertible preferred stock to 36 accredited investors and certain members of our board of directors at a price per share of $2.26 for an aggregate purchase price of $7.0 million.

(4) In March 2017, we issued warrants exercisable for up to an aggregate of 309,389 shares of our common stock, at an exercise price of $2.49 per share to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC, pursuant to that certain placement agency agreement, dated October 7, 2016, as amended and restated on November 23, 2016.

(5) In February 2018, we issued an aggregate of $6.0 million of our convertible notes to 22 accredited investors and certain members of our board of directors.

(6) In November 2018, we issued warrants exercisable for up to an aggregate of 76,847 shares of our common stock, at an exercise price of $6.59 per share to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC, pursuant to that certain placement agency agreement, dated January 18, 2018.

(7) Between November 2018 and February 2019, we issued and sold an aggregate of 4,444,773 shares of our Series B convertible preferred stock to 28 accredited investors and certain members of our board of directors. We issued 1,097,721 shares of our Series B convertible preferred stock upon cancellation of indebtedness, for an aggregate purchase price at the time of conversion, including interest, of $6.6 million and we sold 3,347,052 shares of our Series B convertible preferred stock at a price per share of $7.49 for an aggregate purchase price of approximately $25.1 million.

(8) In April 2019, we issued warrants exercisable for up to an aggregate of 96,128 shares of our common stock, at an exercise price of $8.24 per share, to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC, pursuant to that certain placement agency agreement, dated August 28, 2018.

(9) In November 2019, we issued and sold an aggregate of 1,380,344 shares of our common stock to 12 accredited investors at a per share price of $14.50, for an aggregate purchase price of approximately $20 million.

(10) In December 2019, we issued 17,026 shares of our common stock to an affiliate of Brookline Capital Markets, a division of CIM Securities, LLC, in a net exercise of 20,000 warrant shares pursuant to a warrant issued in March 2017.

The offers, sales and issuances of the securities described in paragraph (1) were deemed to be exempt from registration under the Securities Act in reliance on Rule 701 in that the transactions were under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of such securities were employees, directors or bona fide consultants of the Registrant and received the securities under the 2016 Plan. Appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions had adequate access, through employment, business or other relationships, to information about the Registrant.

The offers, sales and issuances of the securities described in paragraphs (2) through (10) above were deemed to be exempt from registration under the Securities Act in reliance on Section 4(a)(2) of the Securities Act and Rule 506 promulgated under Regulation D as transactions by an issuer not involving a public offering. The recipients of securities in each of these transactions acquired the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. Each of the recipients of securities in these transactions was an accredited investor within the meaning of Rule 501 of Regulation D under the Securities Act and had adequate access, through employment, business or other relationships, to information about the Registrant. No underwriters were involved in these transactions.

Use of Proceeds from Registered Offerings

On May 16, 2019, we completed our initial public offering, or IPO, of our common stock pursuant to which we issued and sold 4,000,000 shares of our common stock at a public offering price of $10.00 per share. All of our common stock issued and sold in the IPO were registered under the Securities Act pursuant to the registration statement on Form S-1 (Registration No. 333-230838), which was declared effective by the SEC on May 16, 2018. We received net proceeds of $34.6 million, after deducting underwriting discounts and commissions and offering costs. The shares began trading on The Nasdaq Global Market on May 14, 2019. Upon completion of the IPO, all of our outstanding shares of convertible preferred stock converted into 7,538,671 shares of our common stock.

As of December 31, 2019, we have used $26.7 million of the net offering proceeds primarily to advance our product candidates through clinical trial programs and for working capital and general corporate purposes.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

ITEM 6. SELECTED FINANCIAL DATA.

The following tables set forth our selected statement of operations data for the years ended December 31, 2019 2018, and 2017 and our selected balance sheet data as of December 31, 2019 and 2018, all of which have been derived from our financial statements appearing elsewhere in this Annual Report. Our historical results are not necessarily indicative of the results that may be expected for any period in the future. You should read the following selected financial data together with the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and the related notes included elsewhere in this Annual Report. The

selected financial data included in this section are not intended to replace the financial statements and are qualified in their entirety by the financial statements and the related notes included elsewhere in this Annual Report.

(in thousands, except share and per share data)	Years Ended December 31, 2019	2018	2017
Summary of Operations Data:			
Operating expenses:			
Research and development	$ 32,350	$ 11,471	$ 3,703
General and administrative	13,232	2,047	582
Total operating expenses	45,582	13,518	4,285
Loss from operations	(45,582)	(13,518)	(4,285)
Other income (expense), net:			
Interest income (expense), net	93	(1,642)	3
Loss on extinguishment of debt	—	(221)	—
Other expense	(24)	(1,140)	—
Total other income (expense), net	69	(3,003)	3
Net loss	$ (45,513)	$ (16,521)	$ (4,282)
Net loss per share: basic and diluted[(1)]	$ (3.55)	$ (3.01)	$ (0.79)
Weighted-average shares used in computing net loss per share: basic and diluted[(1)]	12,831,221	5,483,149	5,406,513

(1) See Notes 1 and 10 to our financial statements included elsewhere in this Annual Report for an explanation of the calculations of our basic and diluted net loss per share and the weighted-average number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31, 2019	2018
Balance Sheet Data:		
Cash and cash equivalents	$ 18,850	$ 18,748
Investments	20,004	—
Working capital	32,056	15,818
Total assets	48,389	20,246
Preferred stock	—	35,410
Accumulated deficit	(66,770)	(21,257)
Total stockholders' (deficit) equity	32,607	(19,592)

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report, our actual results could differ materially from the results described in or implied by these forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against validated molecular targets in indications of high unmet medical need. We focus on molecules and pathways whose role in the disease process is well known based on prior research, but have previously failed to yield successful products due

to poor efficacy and tolerability. Our unique approach to drug development leverages recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on potential use of expedited regulatory pathways. Our first molecular target is aldose reductase, or AR, an enzyme that converts glucose to sorbitol under oxidative stress conditions, and is implicated in multiple diseases. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. The detrimental consequences of AR activation have been well established by decades of prior research. Our AR program currently includes three small molecules, which are all potent and selective inhibitors of AR, but are engineered to have unique tissue permeability profiles to target different disease states, including diabetic complications, heart disease and a rare pediatric metabolic disease. Using similar strategies to our AR inhibitors, or ARI, program, we have also developed a program targeting selective inhibition of phosphatidylinositol 3-kinase, or PI3K, subunits that produced an early-stage oncology pipeline. The result of this unique multifaceted approach to drug development is a portfolio of highly specific and selective product candidates that we believe are significantly de-risked and can move quickly through the development process. We plan to initiate our clinical program in these indications in 2020.

AT-007 is a novel central nervous system, or CNS, penetrant ARI that we are developing for the treatment of galactosemia, a devastating rare pediatric metabolic disease that affects how the body processes a simple sugar called galactose, and for which there is no known cure or approved treatment available. In May 2019, the U.S. Food and Drug Administration, or FDA, granted orphan drug designation to AT-007 for the treatment of galactosemia. We initiated a Phase 1/2 study of AT-007 in galactosemia in June 2019. The study is a double-blind placebo-controlled trial evaluating safety and pharmacokinetics of AT-007 in healthy volunteers, as well as safety, pharmacokinetics and biomarker effects in adult galactosemia patients over 28 days of once daily oral dosing. The key biomarker outcome of the study was reduction in galactitol, an aberrant toxic metabolite of galactose, formed by AR in galactosemia patients.

In January 2020, we announced positive topline results. AT-007 treatment resulted in a statistically significant and robust reduction in plasma galactitol versus placebo in adult galactosemia patients. Reductions in galactitol were dose dependent, with higher concentrations of AT-007 resulting in a greater magnitude of reduction in galactitol. At the highest dose tested (20mg/kg), AT-007 significantly reduced plasma galactitol 45-54% from baseline versus placebo (with a p value of less than 0.01). Galactitol reduction was rapid and sustained over time. No substantial change from baseline was observed in placebo treated patients. AT-007 was well tolerated, with no drug-related adverse events noted to date in galactosemia patients or in the 72 healthy volunteers treated in Part 1 of the trial.

We will continue to characterize AT-007 long-term safety in adult galactosemia patients and intend to initiate a pediatric study.

AT-001 is a novel ARI with broad systemic exposure and peripheral nerve permeability that we are developing for the treatment of diabetic cardiomyopathy, or DbCM, a fatal fibrosis of the heart, for which no treatments are available. We completed a Phase 1/2 clinical trial evaluating AT-001 in approximately 120 patients with type 2 diabetes, in which no drug-related adverse effects or tolerability issues were observed. In September 2019, we announced the initiation of a Phase 3 registrational trial for AT-001 in DbCM. The study, called ARISE-HF, will investigate AT-001's ability to improve or prevent the decline of functional capacity in patients with DbCM at high risk of progression to overt heart failure.

Since inception in 2016, our operations have focused on developing our product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials. We do not have any product candidates approved for sale and have not generated any revenue.

Initial Public Offering

On May 16, 2019, we completed the IPO, in which we issued and sold 4,000,000 shares of our common stock at a public offering price of $10.00 per share, for aggregate gross proceeds of $40.0 million. We received approximately $34.6 million in net proceeds after deducting underwriting discounts and commissions and estimated offering costs. The shares began trading on The Nasdaq Global Market on May 14, 2019. Upon completion of the IPO, all of our outstanding shares of convertible preferred stock, converted into 7,538,671 shares of our common stock.

Prior to the completion of the IPO, we primarily funded our operations with proceeds from the sale of convertible preferred stock. We have incurred significant operating losses since inception in 2016. Our ability to generate product revenue sufficient to achieve profitability depends on the successful development and commercialization of one or more of our product candidates. Our net loss was $45.6 million for the twelve months ended December 31, 2019. As of December 31, 2019, we had an accumulated deficit of $66.8 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future in connection with our ongoing activities. Furthermore, we expect to continue to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses. As of December 31, 2019, we had cash and cash equivalents and short-term investments of $38.9 million.

November 2019 Private Placement

On November 7, 2019, we entered into a securities purchase agreement for the Private Placement with the Purchasers. Pursuant to the securities purchase agreement, the Purchasers purchased 1,380,344 shares of our common stock. The purchase price for each share was $14.50, with net proceeds of approximately $18 million. The closing of the purchase and sale of the securities occurred on November 12, 2019.

January 2020 Secondary Public Offering

In January 2020, we issued and sold 2,741,489 shares of our common stock at a public offering price of $45.50 per share, with an additional 411,223 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares in the Secondary Public Offering. We received aggregate net proceeds, net of underwriting discounts and commissions and estimated offering expenses of $134.8 million.

Components of Our Results of Operations

Revenue

Since inception, we have not generated any revenue and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for our product candidates are successful and result in regulatory approval, or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts and the development of our product candidates, and include:

- employee-related expenses, including salaries, related benefits and stock-based compensation expense for employees engaged in research and development functions;
- fees paid to consultants for services directly related to our product development and regulatory efforts;
- expenses incurred under agreements with contract research organizations, or CROs, as well as contract manufacturing organizations, or CMOs, and consultants that conduct and provide supplies for our preclinical studies and clinical trials;
- costs associated with preclinical activities and development activities;
- costs associated with our technology and our intellectual property portfolio; and

- costs related to compliance with regulatory requirements.

We expense research and development costs as incurred. Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase for the foreseeable future as we continue clinical development for our product candidates and continue to discover and develop additional product candidates. If any of our product candidates enter into later stages of clinical development, they will generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. Historically, we have incurred research and development expenses that primarily relate to the development of AT-001, AT-007 and our ARI program. As we advance our product candidates, we expect to allocate our direct external research and development costs across each of the indications or product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive and finance functions. General and administrative expenses also include professional fees for legal, accounting, auditing, tax and consulting services; travel expenses; and facility-related expenses, which include allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our general and administrative headcount to support our continued research and development and potential commercialization of our product candidates. We also expect to incur increased expenses associated with being a public company, including costs of accounting, audit, legal, regulatory and tax compliance services; director and officer insurance costs; and investor and public relations costs.

Other Income (Expense), Net

Other income (expense), net consists of interest income (expense), net, loss on extinguishment of debt and other expenses. Interest income (expense), net consists primarily of our interest income on our cash and cash equivalents and marketable securities and interest expense related to the convertible promissory notes. Loss on extinguishment of debt consists of a loss on extinguishment related to the conversion of convertible promissory notes into Series B Preferred Stock. Other expense consists of adjustments to the fair value of embedded derivatives associated with certain conversion features of the convertible promissory notes and adjustments to the fair value of the warrant liability in connection with the convertible promissory notes.

Results of Operations

The following table summarizes our results of operations:

(in thousands)	Years Ended December 31, 2019	2018
Operating expenses:		
Research and development	$ 32,350	$ 11,471
General and administrative	13,232	2,047
Total operating expenses	45,582	13,518
Loss from operations	(45,582)	(13,518)
Other (expense) income, net:		
Interest income (expense), net	93	(1,642)
Loss on extinguishment of debt	—	(221)
Other expense	(24)	(1,140)
Other (expense) income, net	69	(3,003)
Net loss	$ (45,513)	$ (16,521)

Research and Development Expenses

The following table summarizes our research and development expenses:

(in thousands)	Year Ended December 31, 2019	2018	Increase
Clinical and pre-clinical	$ 17,436	$ 5,083	$ 12,353
Drug manufacturing and formulation	9,069	4,938	4,131
Personnel expenses (including share-based compensation)	5,490	933	4,557
Regulatory and other	355	517	(162)
Total research and development expenses	$ 32,350	$ 11,471	$ 20,880

Research and development expenses for the year ended December 31, 2019 were $32.4 million, compared to $11.5 million for the year ended December 31, 2018. The increase of approximately $20.9 million was primarily related to increased activity on our clinical trials, including an increase in clinical and pre-clinical expenses of $12.4 million and drug manufacturing and formulation expenses of $4.1 million, personnel expenses of $4.6 million due to an increase in the chief executive officer salary, for which a portion was allocated to research and development, the hiring of research and development personnel, including the chief medical officer, share-based compensation and employee bonuses, and offset by a decrease of regulatory and other expenses of $0.2 million.

General and Administrative Expenses

The following table summarizes our general and administrative expenses:

(in thousands)	Year Ended December 31, 2019	2018	Increase
Personnel expenses (including share-based compensation)	$ 4,871	$ 424	$ 4,447
Legal and professional fees	4,397	853	3,544
Other expenses	3,964	770	3,194
Total general and administrative expenses	$ 13,232	$ 2,047	$ 11,185

General and administrative expenses were $13.2 million for the year ended December 31, 2019, compared to $2.0 million for the year ended December 31, 2019. The increase of approximately $11.2 million was primarily related

to the increase of personnel expenses of $4.4 million due to an increase in the chief executive officer salary, for which a portion was allocated to general and administrative and the hiring of other personnel, including the chief financial officer, and an increase in professional and legal fees of $3.5 million due to the closing of multiple financings and increased IP work, and an increase in other expenses of $3.2 million, primarily due to recruiting efforts for the chief medical officer and rent.

Other Income (Expense), Net

Other income (expense), net was income of approximately $69,000 for the year ended December 31, 2019, compared to expense of $3.0 million for the year ended December 31, 2018. The change from expense to income was primarily related to a the conversion of promissory notes in 2018, resulting in a decrease in non-cash interest expense on convertible promissory notes of $1.6 million, a loss on extinguishment related to the conversion of convertible promissory notes into Series B Preferred Stock of $0.2 million and the removal of the associated fair value of the derivative liability of $1.0 million and warrant liability of $0.2 million related to the promissory notes. Additionally, there was interest income earned on marketable securities of $93,000 in 2019.

Liquidity and Capital Resources

Since our inception through December 31, 2019, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. We expect our existing cash and cash equivalents and short-term investments of $38.9 million as of December 31, 2019, together with the net proceeds from the Secondary Public Offering of approximately $134.8 million, net of underwriting discounts and commissions and estimated offering expenses subsequent to December 31, 2019, will be sufficient to fund our operating expenses and capital expenditure requirements for at least one year from the date of this Annual Report on Form 10-K.

Cash Flows

The following table summarizes our cash flows for each of the periods presented:

	Year Ended December 31,	
(in thousands)	**2019**	**2018**
Net cash used in operating activities	$ (36,307)	$ (11,182)
Net cash used in investing activities	(20,006)	—
Net cash provided by financing activities	56,415	26,653
Net increase (decrease) in cash and cash equivalents	$ 102	$ 15,471

Operating Activities

During the year ended December 31, 2019, operating activities used cash of $36.3 million, primarily comprising cash research and development spending, related to increased clinical and pre-clinical activities, drug manufacturing and formulation development.

During the year ended December 31, 2018, operating activities used cash of $11.2 million of cash, primarily comprising cash research and development spending related to increased clinical and pre-clinical activities, drug manufacturing and formulation development.

Investing Activities

Net cash used in investing activities for the year ended December 21, 3019 was $20.0 million relating to our investment in marketable securities for $20.0 million. For the year ended December 31, 2018, there were no investing activities.

Financing Activities

During the year ended December 31, 2019, net cash provided by financing activities was $56.4 million, primarily from the cash proceeds from the IPO of $37.2 million, net of underwriting costs, and from the issuance of Series B Preferred Stock resulting in $3.1 million cash proceeds, as well as $18.4 million of cash proceeds from the Private Placement.

During the year ended December 31, 2018, net cash provided by financing activities was $26.7 million. Cash proceeds, net of cash issuance costs, from the sale of our Series B Preferred Stock was $21.2 million and cash proceeds, net of cash issuance costs, from the sale of convertible promissory notes was $5.6 million. Cash proceeds from the exercise of stock options were approximately $47,000. The net cash provided by financing activities was partially offset by the payment of deferred financing costs related to the IPO of $0.1 million.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities and clinical trials of our product candidates. We expect that our expenses will increase significantly if and as we:

- continue the ongoing and planned development of our product candidates;
- initiate, conduct and complete any ongoing, anticipated or future preclinical studies and clinical trials for our current and future product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any current or future product candidate for which we may obtain marketing approval;
- seek to discover and develop additional product candidates;
- continue to build a portfolio of product candidates through the acquisition or in-license of drugs, product candidates or technologies;
- maintain, protect and expand our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses that we did not incur as a private company.

Due to the numerous risks and uncertainties associated with the development of our product candidates and programs, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future funding requirements, both near and long-term, will depend on many factors, including:

- the initiation, scope, progress, timing, costs and results of our ongoing and planned clinical trials for our product candidates;

- the outcome, timing and cost of meeting regulatory requirements established by the FDA and other comparable foreign regulatory authorities;
- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions;
- the achievement of milestones or occurrence of other developments that trigger payments under the Columbia Agreements or other agreements we may enter into;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the effect of competing technological and market developments;
- the cost and timing of completion of clinical or commercial-scale manufacturing activities;
- the costs of operating as a public company;
- the extent to which we in-license or acquire other products and technologies;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our product candidates, if approved; and
- the initiation, progress, timing and results of the commercialization our product candidates, if approved, for commercial sale.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through offerings of securities, private equity financing, debt financings, collaborations or other strategic transactions. The terms of financing may adversely affect the holdings or the rights of our stockholders. If we are unable to obtain funding, we may be required to delay, limit, reduce or terminate some or all of our research and product development, product portfolio expansion or future commercialization efforts. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2019:

	Payments Due By Period				
(in thousands)	**Total**	**Less Than 1 Year**	**1 to 3 Years**	**4 to 5 Years**	**More Than 5 Years**
Operating lease commitments[(1)]	$ 2,343	$ 462	$ 1,457	$ 424	$ —
Total	$ 2,343	$ 462	$ 1,457	$ 424	$ —

(1) Represents future minimum lease payments under our operating lease for office space.

Except as disclosed in the table above, we have no long-term debt or capital leases and no material non-cancelable purchase commitments with service providers, as we have generally contracted on a cancelable, purchase-order basis. We enter into contracts in the normal course of business with CROs, CMOs and other third parties for clinical trials, preclinical research studies and testing and manufacturing services. These contracts are cancelable by us upon prior notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation. These payments are not included in the preceding table as the amount and timing of such payments are not known.

We may incur potential contingent payments upon our achievement of clinical, regulatory and commercial milestones, as applicable, or royalty payments that we may be required to make under the 2016 and 2019 Columbia Agreements pursuant to which we have in-licensed certain intellectual property. Due to the uncertainty of the achievement and timing of the events requiring payment under this agreement, the amounts to be paid by us are not fixed or determinable at this time and are excluded from the table above. See the section titled “Business—Exclusive License Agreement with Columbia University.”

Critical Accounting Policies and Significant Judgments and Estimates

Our management’s discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of our financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, costs and expenses and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in greater detail in Note 1 to our financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued Research and Development Expenses

We expense all costs incurred in performing research and development activities. Research and development expenses include materials and supplies, preclinical expenses, manufacturing expenses, contract services and other outside expenses. As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. We make estimates of our accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known to us at that time. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Stock-Based Compensation

We account for our stock-based compensation as expense in the statements of operations based on the awards’ grant date fair values. We account for forfeitures as they occur by reversing any expense recognized for unvested awards.

We estimate the fair value of options granted using the Black-Scholes option pricing model. The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of a public market for our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to us, including stage of product development and life science industry focus. We use the simplified method as allowed by the SEC Staff Accounting Bulletin No. 107, Share-Based Payment, to calculate the expected term for options granted as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as we have never paid dividends and have no current plans to pay any dividends on our common stock. The fair value of stock-based payments is recognized as expense over the requisite service period which is generally the vesting period.

Determination of the Fair Value of Common Stock

As there was no public market for our common stock prior to the IPO on May 16, 2019, the estimated fair value of our common stock prior to May 16, 2019 had been determined by our board of directors, with input from management, considering third party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third party valuation through the date of the option grant. These third party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

In addition to considering the results of these third party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biotechnology industry and trends within the biotechnology industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or sale of our company in light of prevailing market conditions; and
- the analysis of initial public offerings and the market performance of similar companies in the biotechnology industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used different assumptions or

estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Options Granted

The intrinsic value of all outstanding options as of December 31, 2019 was $83.5 million, based on the fair value of our common stock of $27.28 per share, of which approximately $34.9 million related to vested options and approximately $48.6 million related to unvested options.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 1 to our financial statements appearing elsewhere in this Annual Report.

Quantitative and Qualitative Disclosures about Market Risks

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities.

As of December 31, 2019, we had cash, cash equivalents and investments of $38.9 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.S. bank interest rates. Our surplus cash has been invested in interest-bearing savings accounts from time to time. We have not entered into investments for trading or speculative purposes. We do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

As of December 31, 2019, we had no outstanding debt and are therefore not subject to interest rate risk related to debt.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012 permits an “emerging growth company” such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to “opt out” of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities and foreign currency senstivities.

Interest Rate Sensitivity

Our exposure to market risk relates to our cash, cash equivalents and investments of $38.9 million. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Some of the financial instruments in which we invest could be subject to market risk where the interest rates may cause the value of the instruments to fluctuate. To minimize this risk, we intend to

maintain a portfolio which may include cash, cash equivalents and short-term investment securities available-for-sale in a variety of securities

The securities in our investment portfolio are not leveraged and are classified as available-for-sale. These available-for-sale securities are short-term in nature and subject to minimal interest rate risk. All investments have a fixed interest rate and are carried at market value, which approximates cost. We do not use derivative financial instruments in our investment portfolio. We do not believe that a change in interest rates would have a material negative impact on the value of our investment portfolio.

We do not believe that our cash has significant risk of default or illiquidity. While we believe our cash and cash equivalents does not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash at one or more financial institutions that are in excess of federally insured limits. Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

As of December 31, 2019, we had cash and cash equivalents of $18.9 million. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.S. bank interest rates. Our surplus cash has been invested in interest-bearing savings accounts from time to time. We have not entered into investments for trading or speculative purposes. We do not believe an immediate one percentage point change in interest rates would have a material effect on the fair market value of our portfolio, and therefore we do not expect our operating results or cash flows to be significantly affected by changes in market interest rates.

As of December 31, 2019, we had no outstanding debt and are therefore not subject to interest rate risk related to debt.

Foreign Currency Sensitivity

Our primary operations are transacted in U.S. Dollars, however, certain service agreements with third parties are denominated in currencies other than the U.S. Dollar, primarily the Euro. As such, we are subject to foreign exchange risk and therefore, fluctuations in the value of the U.S. Dollar against the Euro may impact the amounts reported for expenses and obligations incurred under such agreements. We do not participate in any foreign currency hedging activities and we do not have any other derivative financial instruments. We did not recognize any significant exchange rate loss during the year ended December 31, 2019. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have a material impact on our financial condition or results of operations.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

The information required by this item is set forth in the consolidated financial statements filed with this report and are herein and incorporated by reference.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Applied Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Applied Therapeutics, Inc. (the Company) as of December 31, 2019 and 2018, the related statements of operations, comprehensive (loss) income, convertible preferred stock and stockholders' (deficit) equity and cash flows for each of the two years in the period ended December 31, 2019, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2017.

New York, New York
March 13, 2020

Applied Therapeutics, Inc.

Balance Sheets

(in thousands except share and per share data)

	As of December 31, 2019	As of December 31, 2018
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 18,850	$ 18,748
Prepaid expenses and other current assets	7,301	1,498
Investments	20,004	—
Total current assets	46,155	20,246
Operating lease right-of-use asset	2,035	—
Security deposits and leasehold improvements	199	—
TOTAL ASSETS	$ 48,389	$ 20,246
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Current portion of operating lease liabilities	356	—
Accounts payable	8,793	3,015
Accrued expenses and other current liabilities	4,950	1,413
Total current liabilities	14,099	4,428
NONCURRENT LIABILITIES:		
Noncurrent portion of operating lease liabilities	1,683	—
Total noncurrent liabilities	1,683	—
Total liabilities	15,782	4,428
Series A convertible preferred stock, $0.0001 par value; 0 shares and 3,093,898 shares authorized at December 31, 2019 and December 31, 2018, respectively; 0 shares and 3,093,898 shares issued and outstanding at December 31, 2019 and December 31, 2018, respectively; liquidation preference of $0 and $7,000 at December 31, 2019 and December 31, 2018, respectively	—	6,254
Series B convertible preferred stock, $0.0001 par value; 0 shares and 7,790,052 shares authorized as of December 31, 2019 and December 31, 2018, respectively; 0 shares and 4,001,848 shares issued and outstanding as of December 31, 2019 and December 31, 2018, respectively; liquidation preference of $0 and $29,964 as of December 31, 2019 and December 31, 2018, respectively	—	29,156
STOCKHOLDERS' EQUITY (DEFICIT):		
Common stock, $0.0001 par value; 100,000,000 and 20,441,982 shares authorized as of December 31, 2019 and December 31, 2018, respectively; 18,531,560 shares and 5,513,531 shares issued and outstanding as of December 31, 2019 and December 31, 2018, respectively	1	—
Additional paid-in capital	99,378	1,665
Accumulated other comprehensive loss	(2)	—
Accumulated deficit	(66,770)	(21,257)
Total stockholders' equity (deficit)	32,607	(19,592)
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)	$ 48,389	$ 20,246

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Operations

(in thousands except share and per share data)

	Year Ended December 31,	
	2019	2018
OPERATING EXPENSES:		
Research and development	$ 32,350	$ 11,471
General and administrative	13,232	2,047
Total operating expenses	45,582	13,518
LOSS FROM OPERATIONS	(45,582)	(13,518)
OTHER INCOME (EXPENSE), NET:		
Interest income (expense), net	93	(1,642)
Loss on extinguishment of debt	—	(221)
Other income (expense)	(24)	(1,140)
Total other income (expense), net	69	(3,003)
Net loss	$ (45,513)	$ (16,521)
Net loss attributable to common stockholders—basic and diluted	$ (45,513)	$ (16,521)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.55)	$ (3.01)
Weighted-average common stock outstanding—basic and diluted	12,831,221	5,483,149

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Comprehensive Income (Loss)

(in thousands except share and per share data)

	Year Ended December 31,	
	2019	2018
Net Loss	$ (45,513)	$ (16,521)
Other comprehensive income (loss)		
Unrealized gain (loss) on marketable securities	(2)	—
Other comprehensive income (loss), net of tax	(2)	—
Comprehensive income (loss), net of tax	$ (45,515)	$ (16,521)

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statement of Convertible Preferred Stock and Stockholders' (Deficit) Equity

(in thousands, except share and per share data)

	Convertible Preferred Stock				Common Stock					
	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		$0.0001 Par Value		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount				
BALANCE, January 1, 2018	3,093,898	$ 6,254	—	$ —	5,458,450	$ —	$ 775	$ (4,736)	$ —	$ (3,961)
Issuance of Series B convertible preferred stock for cash, net of issuance costs of $812	—	—	2,904,127	20,937	—	—	—	—	—	—
Issuance of Series B convertible preferred stock on extinguishment of convertible promissory notes	—	—	1,097,721	8,219	—	—	101	—	—	101
Issuance of common stock warrants in connection with the issuance of convertible promissory notes	—	—	—	—	—	—	242	—	—	242
Issuance of common stock warrants in connection with the issuance of Series B convertible preferred stock	—	—	—	—	—	—	228	—	—	228
Exercise of options for common stock issued under Equity Incentive Plan	—	—	—	—	55,081	—	47	—	—	47
Stock-based compensation expense	—	—	—	—	—	—	272	—	—	272
Net loss	—	—	—	—	—	—	—	(16,521)	—	(16,521)
BALANCE, December 31, 2018	3,093,898	$ 6,254	4,001,848	$ 29,156	5,513,531	$ —	$ 1,665	$ (21,257)	$ —	$ (19,592)
BALANCE, December 31, 2018	3,093,898	$ 6,254	4,001,848	$ 29,156	5,513,531	$ —	$ 1,665	$ (21,257)	$ —	$ (19,592)
Issuance of Series B convertible preferred stock for cash, net of issuance costs of $419	—	—	442,925	2,897	—	—	—	—	—	—
Issuance of common stock warrants in connection with the issuance of Series B convertible preferred stock	—	—	—	—	—	—	80	—	—	80
Conversion of Series A convertible preferred stock into common stock upon closing of the IPO	(3,093,898)	(6,254)	—	—	3,093,898	—	6,254	—	—	6,254
Conversion of Series B convertible preferred stock into common stock upon closing of the IPO	—	—	(4,444,773)	(32,053)	4,444,773	1	32,052	—	—	32,053
Issuance of common stock upon the IPO, net of issuance costs of $5,417	—	—	—	—	4,000,000	—	34,582	—	—	34,582
Exercise of options for common stock issued under Equity Incentive Plan	—	—	—	—	81,988	—	226	—	—	226
Issuance of common stock upon Private Placement, net of issuance costs of $1,667	—	—	—	—	1,380,344	—	18,348	—	—	18,348
Exercise of warrants of common stock	—	—	—	—	17,026	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	6,171	—	—	6,171
Net loss	—	—	—	—	—	—	—	(45,513)	—	(45,513)
Other comprehensive income (loss)	—	—	—	—	—	—	—	—	(2)	(2)
BALANCE, December 31, 2019	—	$ —	—	$ —	18,531,560	$ 1	$ 99,378	$ (66,770)	$ (2)	$ 32,607

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Cash Flows

(in thousands)

	Year Ended December 31,	
	2019	**2018**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (45,513)	$ (16,521)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	6,171	272
Amortization of operating lease right-of-use assets	23	—
Non-cash interest expense	—	1,642
Change in fair value of derivative liability	—	972
Change in fair value of warrant liability	—	168
Loss on extinguishment of debt	—	221
Change in operating lease liability	(19)	—
Changes in operating assets and liabilities:		
Prepaid expenses	(5,922)	(1,179)
Accounts payable	5,751	2,302
Accrued expenses and other current liabilities	3,401	941
Payment of security deposit and leasehold improvements for long-term lease	(199)	—
Net cash used in operating activities	(36,307)	(11,182)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchase of available-for-sale securities	(20,006)	—
Net cash used in investing activities	(20,006)	—
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from issuance of Series B convertible preferred stock, net of cash issuance costs of $340	2,977	21,165
Proceeds from issuance of convertible promissory notes, net of cash issuance costs of $440	—	5,560
Proceeds from issuance of Private Placement stock, net of cash issuance costs of $1,509	18,510	
Payment of IPO costs	(2,498)	(119)
Proceeds from the IPO, net of underwriter commissions	37,200	—
Exercise of stock options for common stock under Equity Incentive Plan	226	47
Net cash provided by financing activities	56,415	26,653
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	102	15,471
Cash and cash equivalents at beginning of period	18,748	3,277
Cash and cash equivalents at end of period	$ 18,850	$ 18,748
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:		
Operating lease right-of-use asset obtained in exchange for operating lease liability	$ 2,096	—
Issuance of warrants in connection with convertible promissory notes	$ —	$ 242
Issuance of warrants in connection with Series B convertible preferred stock	$ 80	$ 228
Issuance of Series B convertible preferred stock upon extinguishment of convertible promissory notes	$	8,219
Derivative liability in connection with issuance of convertible promissory notes	$ —	$ 1,896
Extinguishment of convertible promissory notes	—	4,646
Extinguishment of derivative liability in connection with extinguishment of convertible promissory notes	—	2,868
IPO costs in accrued expenses	$ —	191
Private Placement costs in accrued expenses	135	—
Private Placement costs in accounts payable	27	—
Conversion of Preferred Stock to Equity Following the IPO	$ 38,307	$ —

The Notes to Financial Statements are an integral part of these statements.

NOTES TO UNAUDITED CONSOLIDATED FINANCIAL STATEMENTS

1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Operations and Business

Applied Therapeutics, Inc. (the "Company") is a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against validated molecular targets in indications of high unmet medical need. In particular, the Company is currently targeting treatments for cardiovascular disease, galactosemia and diabetic complications. The Company was incorporated in Delaware on January 20, 2016 and is headquartered in New York, New York.

On May 16, 2019, the Company completed an initial public offering ("IPO") in which the Company issued and sold 4,000,000 shares of its common stock at a public offering price of $10.00 per share, for aggregate gross proceeds of $40.0 million. The Company received net of proceeds $34.6 million, after deducting underwriting discounts and commissions and offering costs. Prior to the completion of the IPO, the Company primarily funded its operations with proceeds from the sale of convertible preferred stock (see Note 10).

In connection with the IPO, the Company effected a 55.2486-for-1 stock split of its issued and outstanding shares of common stock and convertible preferred stock. The stock split became effective on April 26, 2019. Stockholders entitled to fractional shares as a result of the forward stock split received cash payment in lieu of receiving fractional shares. All share and per share amounts presented that relate to periods prior to the stock split in the accompanying financial statements and notes thereto have been retroactively adjusted, where applicable, to reflect this stock split. Shares of common stock underlying outstanding stock options and other equity instruments were proportionately increased and the respective per share value and exercise prices, if applicable, were proportionately decreased in accordance with the terms of the agreements governing such securities.

Upon the closing of the IPO on May 16, 2019, all of the then-outstanding shares of convertible preferred stock automatically converted into 7,538,671 shares of common stock on a one-for-one basis. Subsequent to the closing of the IPO, there were no shares of convertible preferred stock outstanding.

On November 12, 2019, the Company completed a private placement (the "Private Placement"), pursuant to which it issued and sold 1,380,344 shares of the Company's common stock at a price of $14.50 per share, for net proceeds of $18.4 million after deducting underwriting discounts and commissions and offering costs.

On January 28, 2020, the Company completed its secondary public offering (the "Secondary Public Offering"), pursuant to which it issued and sold 2,741,489 shares of common stock at a public offering price of $45.50 per share, with an additional 411,223 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares. The aggregate net proceeds received by the Company from the offering, net of underwriting discounts and commissions and estimated offering expenses, were $134.8 million.

Liquidity

The Company has incurred, and expects to continue to incur, significant operating losses and negative cash flows for at least the next several years as it continues to develop its drug candidates. To date, the Company has not generated any revenue, and it does not expect to generate revenue unless and until it successfully completes development and obtains regulatory approval for one of its product candidates.

Management believes that the Company's existing cash, together with the net proceeds from the S**econdary** Public Offering, will allow the Company to continue its operations for at least 12 months from the issuance date of these financial statements. If the Company is unable to obtain additional funding, the Company will be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect its business prospects, or the Company may be unable to continue operations.

Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

Risks and Uncertainties

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and reliance on third party manufacturers.

Use of Estimates

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Significant Accounting Policies

Fair Value Measurements

Certain assets and liabilities are reported on a recurring basis at fair value. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

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

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Cash and Cash Equivalents

The Company considers all short-term, highly liquid investments, with an original maturity of three months or less, to be cash equivalents. The Company maintains its cash in bank deposit accounts which, at times, may exceed federally insured limits. The Company has not experienced any losses in these accounts and does not believe it is exposed to any significant credit risk on cash and cash equivalents.

Investments

We have investments in marketable debt securities. We determine the appropriate classification of our investments at the date of purchase and reevaluate the classifications at the balance sheet date. Marketable debt securities with maturities of 12 months or less are classified as short-term. Marketable debt securities with maturities greater than 12 months are classified as long-term. The Company’s marketable securities are accounted for as available for sale (“AFS”). AFS securities are reported at fair value. Unrealized gains and losses, after applicable income taxes, are

reported in accumulated other comprehensive income/(loss). Realized gains or losses on the sale of marketable securities are determined using the specific identification method and are recorded as a component of other income (expense), net.

We conduct an other-than-temporary impairment ("OTTI") analysis on a quarterly basis or more often if a potential loss-triggering event occurs. We consider factors such as the duration, severity and the reason for the decline in value, the potential recovery period and whether we intend to sell. For AFS securities, we also consider whether (i) it is more likely than not that we will be required to sell the debt securities before recovery of their amortized cost basis and (ii) the amortized cost basis cannot be recovered as a result of credit losses.

Leases

At the inception of an arrangement, we determine if an arrangement is, or contains, a lease based on the unique facts and circumstances present in that arrangement. Lease classification, recognition, and measurement are then determined at the lease commencement date. For arrangements that contain a lease we (i) identify lease and non-lease components, (ii) determine the consideration in the contract, (iii) determine whether the lease is an operating or financing lease; and (iv) recognize lease ROU assets and liabilities. Lease liabilities and their corresponding ROU assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable and as such, we use our incremental borrowing rate based on the information available at the lease commencement date, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

Most leases include options to renew and, or, terminate the lease, which can impact the lease term. The exercise of these options is at our discretion and we do not include any of these options within the expected lease term as we are not reasonably certain we will exercise these options. We have elected to combine lease components (for example fixed payments including rent) with non-lease components (for example, non-dedicated parking and common-area maintenance costs) on our real estate asset classes.

Fixed, or in substance fixed, lease payments on operating leases are recognized over the expected term of the lease on a straight-line basis. Fixed lease expense on operating leases is recognized within operating expenses within our consolidated statements of operations. We have an operating leases for our corporate office. We have elected the short-term lease exemption and, therefore, do not recognize a ROU asset or corresponding liability for lease arrangements with an original term of 12 months or less. Leasehold improvements and assets under financing lease arrangements are amortized over the lesser of the asset's estimated useful life or the term of the respective lease. Maintenance costs are expensed as incurred.

Operating leases are included in operating lease right-of-use asset, current portion of operating lease liabilities, and noncurrent portion of operating lease liabilities in our consolidated balance sheet as of December 31, 2019.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in the statement of stockholders' (deficit) equity as a reduction of proceeds generated as a result of the offering. Should a planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statement of operations.

Upon closing the IPO in May 2019, $2.6 million in deferred offering costs were reclassified from prepaid and other current assets and recorded against the IPO proceeds reducing additional paid-in capital. As of December 31, 2019, the Company did not have any deferred offering costs recorded in prepaid and other current assets.

Common Stock Valuation

For all periods prior to the IPO, the Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation* (the "Practice Aid"), to estimate the fair value of its common stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's common stock at the time of, and the likelihood of, achieving a liquidity event, such as an IPO or sale. Significant changes to the key assumptions used in the valuations could result in different fair values of common stock at each valuation date.

Convertible Preferred Stock

For all periods prior to the IPO, the Company recorded shares of its convertible preferred stock at their respective fair values on the dates of issuance less issuance costs. The Company classified shares of its convertible preferred stock outside of stockholders' deficit when the redemption of such units or shares is outside the Company's control. The Company did not adjust the carrying values of the convertible preferred units or convertible preferred stock to the liquidation preferences of such units or shares until such time as a deemed liquidation event is probable of occurring.

Research and Development

The Company expenses all costs incurred in performing research and development activities. Research and development expenses include salaries and other related costs, materials and supplies, preclinical expenses, manufacturing expenses, contract services and other outside expenses. As part of the process of preparing the financial statements, the Company is required to estimate their accrued research and development expenses. The Company makes estimates of the accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known at that time. In addition, there may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense in which case such amounts are reflected as prepaid expenses and other current assets. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts the accrual or the amount of prepaid expenses accordingly. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized in prepaid expenses and other current assets. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

General and Administrative

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in the Company's executive and finance functions. General and administrative expenses also include professional fees for legal, accounting, auditing, tax and consulting services; travel expenses; and facility-related expenses, which include allocated expenses for rent and maintenance of facilities and other operating costs.

Stock-Based Compensation

The Company accounts for its stock-based compensation as expense in the statements of operations based on the awards' grant date fair values. The Company accounts for forfeitures as they occur by reversing any expense recognized for unvested awards.

The Company estimates the fair value of options granted using the Black-Scholes option pricing model. The Black-Scholes option pricing model requires inputs based on certain subjective assumptions, including (a) the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the lack of a public market for the Company's common stock and a lack of company-specific

historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The computation of expected volatility is based on the historical volatility of a representative group of companies with similar characteristics to the Company, including stage of product development and life science industry focus. The Company uses the simplified method as allowed by the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin ("SAB") No. 107, Share-Based Payment, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The expected dividend yield is assumed to be zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The fair value of stock-based payments is recognized as expense over the requisite service period which is generally the vesting period.

Income Taxes

The Company uses the asset and liability method of accounting for deferred income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities at currently enacted tax rates. These temporary differences primarily relate to net operating loss carryforwards available to offset future taxable income. Valuation allowances are established, if necessary, to reduce a deferred tax asset to the amount that will more likely than not be realized.

The Company recognizes tax liabilities from an uncertain tax position only if it is more likely than not that the tax position will not be sustained upon examination by the taxing authorities, based on the technical merits of the tax position. There are no uncertain tax positions that have been recognized in the accompanying financial statements. The Company is required to file tax returns in the U.S. federal jurisdiction and in the state of New York. The Company's policy is to recognize interest and penalties related to uncertain tax benefits, if any, as part of income tax expense. No such interest and penalties have been accrued as of December 31, 2019 and 2018.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss available to common stockholders by the weighted-average common stock outstanding. Diluted net loss per share is calculated similarly, except that it includes the dilutive effect of the assumed exercise of securities, including outstanding warrants and the effect of shares issuable under the Company's stock-based compensation plan, if such effect is dilutive.

Segment Information

Operating segments are defined as components of an enterprise for which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company and the Company's chief operating decision-maker, the Company's chief executive officer, views the Company's operations and manages its business as a single operating segment, which is the business of discovering and developing its product candidates.

Recently Adopted Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") No. 2016-02, *Leases (Topic 842)*, which requires an entity to recognize assets and liabilities arising from a lease for both financing and operating leases on their balance sheet date ("ASU No. 2016-02"). ASU No. 2016-02 is effective for fiscal years beginning after December 15, 2018. In July 2018, an amendment was made that allows companies the option of using the effective date of the new standard as the initial application date (at the beginning of the period in which the new standard is adopted, rather than at the beginning of the earliest comparative period). This update includes a short-term lease exception for leases with a term of 12 months or less, in which a lessee can make an

accounting policy election not to recognize the associated lease assets and lease liabilities on its balance sheet. Additionally, in March 2019, the FASB issued ASU 2019-01, *Leases (Topic 842): Codification Improvements* ("ASU No. 2019-01"). ASU No. 2019-01 clarifies the transition guidance related to interim disclosures provided in the year of adoption. Lessees will continue to differentiate between finance leases (previously referred to as capital leases) and operating leases, using classification criteria that are substantially similar to the previous guidance. For lessees, the recognition, measurement, and presentation of expenses and cash flows arising from a lease did not significantly change from previous U.S. GAAP. The modified retrospective method includes several optional practical expedients that entities may elect to apply, as well as transition guidance specific to nonstandard leasing transactions. The Company adopted Topic 842 on January 1, 2019 using a cumulative-effect adjustment on the effective date of the standard, for which comparative periods are presented in accordance with the previous guidance under ASC 840.

In adopting Topic 842, the Company elected to utilize the available package of practical expedients permitted under the transition guidance within the new standard, which does not require the reassessment of the following: i) whether existing or expired arrangements are or contain a lease; ii) the lease classification of existing or expired leases; and iii) whether previous initial direct costs would qualify for capitalization under the new lease standard. Additionally, the Company made an accounting policy election not to recognize assets or related lease liabilities with a lease term of twelve months or less in its balance sheet.

The adoption of this standard did not have an impact on the Company's balance sheet as all of the Company's leases upon adoption were for terms that were less than 12 months. Additionally, the adoption of this standard did not have a material impact on the Company's statements of operations or condensed statement of cash flows. On August 6, 2019 the Company entered into a lease for approximately 6,579 square feet of new office space in New York City (the "Lease"). The Lease commenced upon delivery of the premise after certain improvements were made, which was on October 31, 2019 (the "Commencement Date"), for a five-year period. Under the Lease, the Company pays monthly rent of approximately $38,000 for the first year following the Commencement Date, and such rent will increase by a nominal percentage every year following the first anniversary of the Commencement Date. The Company also pays a real estate tax escalation, as additional rent, over a base year. The commencement of the Lease caused the Company to record a right-of-use lease asset of $2.0 million with a corresponding lease liabilities totaling $2.0 million on the balance sheet. Refer to Note 11, *Leases*, for further details on our adoptions of the new standard.Total lease obligation over the term of the lease is approximately $2.4 million.

Recently Issued Accounting Pronouncements

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*, which eliminates, modifies, and adds disclosure requirements on fair value measurements. The standard is effective for annual periods beginning after December 15, 2019, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact the adoption of ASU 2018-13 will have on its financial statements.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes: Simplifying the Accounting for Income Taxes.* The new standard intended to simplify the accounting for income taxes by eliminating certain exceptions related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The standard is effective for annual periods beginning after December 15, 2020 and interim periods within, with early adoption permitted. Adoption of the standard requires certain changes to primarily be made prospectively, with some changes to be made retrospectively. The Company is currently evaluating the impact adoption of ASU 2019-12 will have on its financial statements.

The FASB issued authoritative guidance that amends guidance on reporting credit losses for assets, including available-for-sale marketable securities and any other financial assets not excluded from the scope that have the contractual right to receive cash. For available-for-sale marketable securities, credit losses should be measured in a manner similar to current generally accepted accounting standards; however, ASU 2016-13, *Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, will require that credit losses be

presented as an allowance rather than as a write-down. We are currently in the process of evaluating the impact of this guidance on our financial statements.

2. LICENSE AGREEMENT

Columbia University

In October 2016, the Company entered into a license agreement (the " 2016 Columbia Agreement") with The Trustees of Columbia University ("Columbia University") to obtain an exclusive royalty-bearing sublicensable license in respect to certain patents. As part of the consideration for entering into the 2016 Columbia Agreement, the Company issued to Columbia University shares equal to 5% of its outstanding common stock on a fully diluted basis at the time of issue. The common stock had a fair value of $0.5 million at the time of issuance. The Company will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2016 Columbia Agreement. The Company will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on the Company's, its affiliates' and its sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, the Company is required to make specified annual minimum royalty payments to Columbia University, which is contingent upon the approval of the licensed products, in the mid six figures beginning on the 10th anniversary of the effective date of the 2016 Columbia Agreement. The Company has not granted any sublicenses under the 2016 Columbia Agreement. However, if the Company sublicenses the rights granted under the 2016 Columbia Agreement to one or more third parties, it will be required to pay Columbia University a portion of the net sublicensing revenue received from such third parties, at percentages between 10% and 20%, depending on the stage of development at the time such revenue is received from such third parties.

The 2016 Columbia Agreement will terminate upon the expiration of all the Company's royalty payment obligations in all countries. The Company may terminate the 2016 Columbia Agreement for convenience upon 90 days' written notice to Columbia University. At its election, Columbia University may terminate the 2016 Columbia Agreement, or convert the licenses granted to the Company into non-exclusive, non-sublicensable licenses, in the case of (a) the Company's uncured material breach upon 30 days' written notice (which shall be extended to 90 days if the Company is diligently attempting to cure such material breach), (b) the Company's failure to achieve the specified development and funding milestone events, or (c) the Company's insolvency.

In January 2019, the Company entered into a second license agreement with Columbia University (the "2019 Columbia Agreement"). Pursuant to the 2019 Columbia Agreement, Columbia University granted the Company a royalty-bearing, sublicensable license that is exclusive with respect to certain patents, and non-exclusive with respect to certain know-how, in each case to develop, manufacture and commercialize PI3k inhibitor products. The license grant is worldwide. Under the 2019 Columbia Agreement, the Company is obligated to use commercially reasonable efforts to research, discover, develop and market licensed products for commercial sale in the licensed territory, and to comply with certain obligations to meet specified development and funding milestones within defined time periods. Columbia University retains the right to conduct, and grant third parties the right to conduct, non-clinical academic research using the licensed technology; provided that such research is not funded by a commercial entity or for-profit entity or results in rights granted to a commercial or for-profit entity. As consideration for entering into the 2019 Columbia Agreement, the Company made a nominal upfront payment to Columbia University. The Company will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2019 Columbia Agreement. The Company will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on the Company's, its affiliates' and its sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, the Company is required to make specified annual minimum royalty payments to Columbia University, which is contingent upon the approval of the licensed products, in the mid-six figures beginning on the tenth anniversary of the effective date of the 2019 Columbia Agreement.

The Company has not granted any sublicenses under the 2019 Columbia Agreement. However, if the Company sublicenses the rights granted under the 2019 Columbia Agreement to one or more third parties, it will be required to pay Columbia University a portion of the net sublicensing revenue received from such third parties, at percentages between 10% and 50%, depending on the stage of development at the time such revenue is received from such third parties. The 2019 Columbia Agreement will terminate upon the expiration of all the Company's royalty payment obligations in all countries. The Company may terminate the 2019 Columbia Agreement for convenience upon 90 days' written notice to Columbia University. At its election, Columbia University may terminate the 2019 Columbia Agreement, or convert the licenses granted to the Company into non-exclusive, non-sublicensable licenses, in the case of (a) the Company's uncured material breach upon 30 days' written notice (which shall be extended to 90 days if the Company is diligently attempting to cure such material breach), (b) the Company's failure to achieve the specified development and funding milestone events, or (c) the Company's insolvency.

In March 2019, and in connection with the 2016 Columbia Agreement, the Company entered into a research services agreement (the "2019 Columbia Research Agreement") with Columbia University with the purpose of analyzing structural and functional changes in brain tissue in an animal model of galactosemia, and the effects of certain compounds whose intellectual property rights were licensed to the Company as part of the 2016 Columbia Agreement on any such structural and functional changes. The 2019 Columbia Research Agreement has a term of 12 months from its effective date; provided that the Company can terminate the 2019 Columbia Research Agreement without cause with at least 30 days' prior written notice. The services covered by the 2019 Columbia Research Agreement will be performed by Columbia University in two parts consisting of six months. The decision to proceed with Part 2 of the 2019 Columbia Research Agreement shall be made solely by the Company and will be contingent on the success of the research performed in Part 1. In consideration for the services performed by Columbia University in Part 1, the Company will be required to pay $0.1 million to Columbia University for staffing, supplies and indirect costs. If the Company decides to continue the research defined in Part 2, the Company will be required to pay an additional $0.2 million to Columbia University.

On October 3, 2019, and in connection with the 2019 Columbia Agreement, the Company entered into a research services agreement (the "PI3k Columbia Research Agreement" and collectively with the 2016 Columbia Agreement, 2019 Columbia Agreement and 2019 Research Agreement, the "Columbia Agreements") with Columbia University with the purpose of analyzing PI3k inhibitors for the treatment of lymphoid malignancies. The research service agreement has a term of 18 months from is effective date; provided that the Company can terminate the research service agreement without cause with at least 30 days prior written notice. Midway through the study period, the Company and Columbia University will review the results of all completed and in progress research and determine whether the research will continue. In consideration for the services performed by Columbia University, the Company will be required to pay $0.4 million to Columbia University for staffing, supplies and indirect costs.

During the years ended December 31, 2019 and 2018, the Company recorded $0.1 million and $0.5 million in research and development expense, respectively, and $0.5 million and $0.3 million, respectively, in general and administrative expense related to the Columbia Agreements. In aggregate, the Company has incurred $1.9 million in expense from the execution of the Columbia Agreements through December 31, 2019.

As of December 31, 2019, the Company had $0.1 million due to Columbia University included in accrued expenses and $0.1 million included in accounts payable. As of December 31, 2018, the Company had $0.1 million due to Columbia University included in accrued expenses and $0.1 million included in accounts payable.

3. FAIR VALUE MEASUREMENTS

The following table summarizes, as of December 31, 2019, the Company's financial assets and liabilities that are measured at fair value on a recurring basis, according to the fair value hierarchy described in the significant accounting

policies section. As of December 31, 2018, the Company did not have financial assets or liabilities that are measured at fair value on a recurring basis, aside from cash which was level 1 (in thousands).

	As of December 31, 2019			
	Level 1	Level 2	Level 3	Total
Cash	$ 18,783	$ —	$ —	$ 18,783
Money market funds	67	—	—	67
Total cash and cash equivalents	$ 18,850	$ —	$ —	$ 18,850
Commercial paper and corporate bonds	—	7,520	—	7,520
U.S. government agency debt securities	—	12,484	—	12,484
Total marketable securities	$ —	$ 20,004	$ —	$ 20,004
Total financial assets measured at fair value on a recurring basis	$ 18,850	$ 20,004	$ —	$ 38,854

Investments in commercial paper, corporate bonds, and U.S. government agency debt securities have been classified as Level 2 as they are valued using quoted prices in less active markets or other directly or indirectly observable inputs. Fair values of corporate bonds and U.S. government agency debt securities were derived from a consensus or weighted average price based on input of market prices from multiple sources at each reporting period. With regard to commercial paper, all of the securities had high credit ratings and one year or less to maturity; therefore, fair value was derived from accretion of purchase price to face value over the term of maturity or quoted market prices for similar instruments if available. During the period ended December 31, 2019, there were no transfers of financial assets between Level 1 and Level 2.

Derivative Liability

The Company's convertible promissory notes issued on February 5, 2018 (the "2018 Notes") (see Note 4), contained certain features which met the criteria to be bifurcated and accounted for separately from the 2018 Notes (the "Derivative Liability"). The Derivative Liability was recorded at fair value of $1.9 million upon the issuance of the 2018 Notes and was subsequently remeasured at fair value at each reporting period and immediately before extinguishment. Changes in the fair value of the Derivative Liability were recognized as a component of other income (expense), net in the statement of operations.

The Derivative Liability was initially valued and remeasured using a "with-and-without" method. The "with-and-without" methodology involves valuing the whole instrument on an as-is basis and then valuing the instrument without the individual embedded derivative. The difference between the entire instrument with the embedded derivative compared to the instrument without the embedded derivative is the fair value of the derivative, recorded as the Derivative Liability. The Derivative Liability is settled when the underlying debt instrument is settled either through conversion or extinguishment into equity at a variable price, which is a redemption feature, or held to maturity. In November 2018, the Derivative Liability was settled in connection with the extinguishment of the 2018 Notes.

Warrant Liability

In connection with the issuance of the 2018 Notes, the Company had a contingent obligation to issue common stock warrants ("2018 Notes Warrants") upon the conversion of the 2018 Notes into Series B convertible preferred stock ("Series B Preferred Stock") (see Note 6 and Note 7). As the obligation to issue the 2018 Notes Warrants was not initially for a fixed number of warrants, it was recorded as a liability (the "Warrant Liability") at fair value of $0.1 million upon the issuance of the 2018 Notes and was subsequently remeasured at fair value each reporting period and immediately before the 2018 Notes were extinguished. Changes in the fair value of the Warrant Liability were recognized in other income (expense), net in the statement of operations. In November 2018, in connection with the conversion of the 2018 Notes into Series B Preferred Stock, the 2018 Notes Warrants were issued and reclassified to equity.

The 2018 Notes Warrants were initially valued and remeasured using a Black-Scholes option pricing model with the range of assumptions as follows:

Contractual term (in years)	10.0
Volatility	74.48% - 76.56%
Risk-free interest rate	2.85% - 3.20%
Dividend yield	0.00%

The following table provides a roll forward of the aggregate fair values of the Company's Derivative Liability and Warrant Liability, for which fair value is determined using Level 3 inputs (in thousands):

	Derivative Liability	Warrant Liability
Balance as of January 1, 2018	$ —	$ —
Initial fair value of Derivative Liability	1,896	—
Initial fair value of Warrant Liability	—	74
Change in fair value	972	168
Extinguishment of Derivative Liability in connection with extinguishment of 2018 Notes	(2,868)	—
Reclassification of Warrant Liability into 2018 Notes Warrants	—	(242)
Balance as of December 31, 2018	$ —	$ —

The inputs utilized by management to value the Derivative Liability and 2018 Notes Warrants are highly subjective. The assumptions used in calculating the fair value of the Derivative Liability and 2018 Notes Warrants represent the Company's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and the Company uses different assumptions, the fair value of the Derivative Liability and 2018 Notes Warrants may be materially different in the future.

4. INVESTMENTS

Marketable Securities

Marketable securities, which the Company classifies as available-for-sale securities, primarily consist of high quality commercial paper, corporate bonds, and U.S. government debt obligations. Marketable securities with remaining effective maturities of twelve months or less from the balance sheet date are classified as short-term; otherwise, they are classified as long-term on the consolidated balance sheets.

The following tables provide the Company's marketable securities by security type (in thousands):

	As of December 31, 2019			
	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Commercial Paper and corporate bonds	$ 7,540	$ —	$ (20)	$ 7,520
US government agency debt security	12,466	19	(1)	12,484
Total	$ 20,006	$ 19	$ (21)	$ 20,004

Contractual maturities of the Company's marketable securities are summarized as follows (in thousands):

	As of December 31, 2019			
	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Due in one year or less	$ 20,006	$ 19	$ (21)	$ 20,004
Total	$ 20,006	$ 19	$ (21)	$ 20,004

At December 31, 2019, the Company had $19 thousand of gross unrealized gains and $21 thousand of gross unrealized losses primarily due to fluctuations in the fair value of certain U.S. government agency debt securities.

During the year ended December 30, 2019, the Company recorded $1 thousand of net realized gains from the sale of marketable securities.

As of December 31, 2019, we did not intend to sell and it was not likely that we would be required to sell these investments before recovery of their amortized cost basis, which may be at maturity. Unrealized losses related to these investments are primarily due to interest rate fluctuations as opposed to changes in credit quality. Therefore, as of December 31, 2019, we have recognized no other-than-temporary impairment loss.

5. CONVERTIBLE PROMISSORY NOTES

On February 5, 2018, the Company issued the 2018 Notes in the aggregate principal amount of $6.0 million. The 2018 Notes bore interest at a rate of 15.0% per annum, were unsecured and were due and payable, including accrued interest, on August 8, 2019. In the event of a qualified sale of preferred stock to one or more investors resulting in gross proceeds to the Company of at least $8.0 million, all principal and accrued and unpaid interest under the 2018 Notes was automatically convertible into a number of shares of the Company's preferred stock issued in such a financing equal to the outstanding principal and accrued but unpaid interest under the 2018 Notes, divided by an amount equal to 80% of the lowest price per share of the preferred stock sold in the financing. In the event of a corporate transaction or change of control event, the 2018 Notes contained a put option whereby the Company was required to pay to the holders of 2018 Notes an amount equal to (i) the principal amount then outstanding under the 2018 Notes plus any accrued but unpaid interest, plus (ii) an amount equal to 30% of the outstanding principal amount.

The terms of the 2018 Notes provided that (i) all outstanding principal and interest was due and payable in cash upon an event of acceleration, as defined in the 2018 Notes agreement; (ii) amounts outstanding under the 2018 Notes were not prepayable without the written consent of the holders of more than 50% of the outstanding principal of the 2018 Notes, and in addition to the balance the Company will prepay, the Company will also pay the noteholders an amount equal to 15% of the principal amount of the 2018 Notes that the Company is prepaying; and (iii) with respect to subordination, the Company has no outstanding indebtedness for borrowed money or any other liabilities, other than accounts payable arrangements with vendors entered into in the ordinary course of business and consistent with usual trade terms and will not issue or incur additional indebtedness for borrowed money while the 2018 Notes remain outstanding. There were no financial or negative covenants associated with the 2018 Notes.

The Derivative Liability represents the conversion feature in the event of a qualified financing and the put option, which each met the definition of an embedded derivative and were required to be combined and accounted for as a separate unit of accounting. The Company recorded the issuance-date fair value of the Derivative Liability of $1.9 million as a debt discount and Derivative Liability in the Company's balance sheet.

In connection with the 2018 Notes, the Company paid legal costs and bank fees of $0.4 million and was obligated to issue the 2018 Notes Warrants (see Note 3 and Note 7) with an initial fair value of $0.1 million, which were capitalized and recorded as a debt discount. The debt discount, which included legal costs, bank fees, the Derivative Liability and 2018 Notes Warrants, was amortized using the effective interest method over the term of the loan. The

Company recognized interest expense of $1.6 million, including amortization of the debt discount of $0.9 million, during the year ended December 31, 2018 in connection with the 2018 Notes.

In November 2018, in connection with the Company's issuance and sale of Series B Preferred Stock, all of the outstanding principal and accrued interest under the 2018 Notes, totaling $6.6 million, was automatically converted into 1,097,721 shares of Series B Preferred Stock at a price equal to 80% of the $7.49 per share price paid by investors in the Series B Preferred Stock financing.

The Company accounted for the conversion of the 2018 Notes as a debt extinguishment and recognized a loss on extinguishment of debt of $0.2 million within other income (expense), net in the Company's statement of operations and $0.1 million within additional paid-in-capital related to the amount of unpaid and accrued interest as of the extinguishment date that was not converted into Series B Preferred Stock. The loss on extinguishment was calculated as the difference between (i) the fair value of the 1,097,721 shares of Series B convertible preferred stock issued to settle the 2018 Notes of $8.2 million and (ii) the carrying value of the 2018 Notes, net of the unamortized debt discount, of $5.1 million plus the then-current fair value of the Derivative Liability associated with the 2018 Notes at the time of the extinguishment of $2.9 million.

6. PREPAID EXPENSE AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2019	December 31, 2018
Deferred offering costs	$ —	$ 310
Prepaid research and development expenses	5,872	1,044
Prepaid rent expenses	142	65
Prepaid insurance expenses	1,196	1
Other prepaid expenses and current assets	91	78
Total prepaid expenses & other current assets	$ 7,301	$ 1,498

7. ACCRUED EXPENSE AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2019	December 31, 2018
Accrued pre-clinical and clinical expenses	$ 4,287	$ 865
Accrued professional fees	345	312
Accrued compensation and benefits	0	56
Accrued patent expenses	54	126
Other	264	54
Total accrued expenses & other current liabilities	$ 4,950	$ 1,413

8. STOCK-BASED COMPENSATION

Equity Incentive Plans

In May 2019, the Company's board of directors (the "Board") adopted its 2019 Equity Incentive Plan ("2019 Plan"), which was subsequently approved by its stockholders and became effective on May 13, 2019, with 1,749,192 shares reserved to grant under the plan. As a result, no additional awards under the Company's 2016 Equity Incentive Plan, as amended (the "2016 Plan") will be granted and all outstanding stock awards granted under the 2016 Plan that are

repurchased, forfeited, expired or are cancelled will become available for grant under the 2019 Plan in accordance with its terms. The 2016 Plan will continue to govern outstanding equity awards granted thereunder.

The 2019 Plan provides for the issuance of incentive stock options ("ISOs") to employees, and for the grant of nonstatutory stock options ("NSOs"), stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other forms of stock awards to the Company's employees, officers and directors, as well as non- employees, consultants and affiliates to the Company. Under the terms of the 2019 Plan, stock options may not be granted at an exercise price less than fair market value of the Company's common stock on the date of the grant. The 2019 Plan will be administered by the Compensation Committee of the Company's Board.

Initially, subject to adjustments as provided in the 2019 Plan, the maximum number of the Company's common stock that may be issued under the 2019 Plan is 4,530,000 shares, which is the sum of (i) 1,618,841 new shares, plus (ii) the number of shares (not to exceed 2,911,159 shares) that remained available for the issuance of awards under the 2016 Plan, at the time the 2019 Plan became effective, and (iii) any shares subject to outstanding stock options or other stock awards granted under the 2016 Plan that are forfeited, expired, or reacquired. The 2019 Plan provides that the number of shares reserved and available for issuance under the 2019 Plan will automatically increase each January 1, beginning on January 1, 2020, by 5% of the outstanding number of shares of common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Board. Subject to certain changes in capitalization of the Company, the aggregate maximum number of shares of common stock that may be issued pursuant to the exercise of ISOs shall be equal to 13,000,000 shares of common stock. Stock options awarded under the 2019 Plan expire 10 years after grant and typically vest over four years.

As of December 31, 2019, there were 368,124 shares of common stock available for future issuance under the 2019 Plan.

Stock-Based Compensation Expense

Total stock-based compensation expense recorded for employees, directors and non-employees (in thousands):

	Year Ended December 31,	
	2019	2018
Research and development	$ 2,762	$ 140
General and administrative	3,409	132
Total stock-based compensation expense	$ 6,171	$ 272

During the year ended December 31, 2019, and 2018 the Company granted options to purchase 2,969,945 and 995,633 shares of common stock, respectively. The weighted-average fair value of options granted during the year ended December 31, 2019 and 2018 was $5.68 per share and $1.54 per share, respectively. As of December 31, 2019 and 2018, the total unrecognized stock-based compensation balance for unvested options was $12.5 million and $1.3 million, respectively, which is expected to be recognized over 1.7 and 2.1 years, respectively. The total fair value of options vested during the year ended December 31, 2019 and 2018 was $3.5 million and approximately $40,000, respectively.

The following table summarizes the information about options outstanding at December 31, 2019 (in thousands, except share and per share data):

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2018	1,202,979	$ 1.35	9.14	$ 4,026
Options granted	2,969,945	6.57		
Options exercised	(81,988)	2.77		—
Forfeited	(11,048)	4.70		
Expired	—	—		
Outstanding at December 31, 2019	4,079,888	$ 5.11	8.26	$ 82,327
Exercisable at December 31, 2019	1,447,191	$ 2.78	8.45	$ 34,818
Nonvested at December 31, 2019	2,632,697	$ 6.39	8.15	$ 47,508

In April 2019, the Company modified certain stock options with service-based conditions that were originally granted under the 2016 Plan. The modification resulted in the vesting for these options to accelerate. There was no incremental stock-based compensation expense as a result of this modification as the fair-value-based measures of the modified awards immediately after the modification were less than the fair-value-based measures of the original awards immediately before the modification.

Valuation of Stock Options Granted to Employees that Contain Service Conditions Only

The fair value of each option award granted with service-based vesting is estimated on the date of the grant using the Black-Scholes option valuation model based on the weighted average assumptions noted in the table below for those options granted in the years ended December 31, 2019 and 2018.

	Year Ended December 31,	
	2019	2018
Expected term (in years)	5.7	5.9
Volatility	72.54 %	71.78 %
Risk-free interest rate	2.17 %	2.71 %
Dividend yield	0.00 %	0.00 %

Stock Options Granted to Employees that Contain Service, Performance and Market Conditions

Included in the stock options granted during the year ended December 31, 2019 were 159,501 stock options that contain service-, performance- and market-based vesting conditions granted to the Company's interim Chief Financial Officer ("CFO") with a fair value at the grant date of $0.5 million, valued using the Monte-Carlo simulation model. The derived service period, calculated using the Monte-Carlo simulation model, ranged from one day to three years. The assumptions used in the Monte-Carlo simulation model were as follows:

	Year Ended December 31, 2019
Time to expiration (in years)	10.0
Volatility	68.54 %
Risk-free interest rate	2.64 %
Dividend yield	0.00 %
Cost of equity	24.00 %
Fair value of underlying common stock (as of valuation date)	$ 5.85

The compensation expense for these awards is recognized over the derived service period, or, if earlier, until the vesting condition is met.

The condition for the performance-based stock options was based on the Company's completion of its IPO and the condition for the market-based stock options was based on the future price of the Company's common stock trading at or above a specified threshold. During the year ended December 31, 2019, 79,778 of the stock options containing service-, and performance-based vesting conditions were vested following the satisfaction of service- and performance-based conditions.

In May 2019, the Company entered into a severance agreement, effective on May 31, 2019 ("Termination Date"), with the interim CFO. As part of this severance arrangement and as of the Termination Date, the Company accelerated the vesting of 79,723 unvested options, which were originally granted to the former CFO under the 2016 Plan. As a result of this modification, the Company recorded stock-based compensation expense of $0.6 million included in general and administrative expense for the year ended December 31, 2019. The Company accounted for this modification as a Type III modification since, at the modification date, the expectation of the award vesting changed from improbable to probable. As a result, the stock-based compensation expense recognized was based on the modification-date fair value.

As of December 31, 2019 all stock options containing service-, performance-, and market-based vesting conditions were vested.

During the year ended December 31, 2019, the Company incurred $0.7 million in stock-based compensation expense relating to the vesting of stock options containing service-, performance- and market-based vesting conditions, which includes the stock-based compensation expense resulting from the modification of these options in May 2019 and were included in general and administrative expense as of December 31, 2019.

2019 Employee Stock Purchase Plan

In May 2019, the Company’s Board and its stockholders approved the 2019 Employee Stock Purchase Plan (the “2019 ESPP”), which became effective as of May 13, 2019. The ESPP is intended to qualify as an “employee stock purchase plan” within the meaning of Section 423 of the U.S. Internal Revenue Code of 1986, as amended. The number of shares of common stock initially reserved for issuance under the ESPP was 180,000 shares. The ESPP provides for an annual increase on the first day of each year beginning in 2020 and ending in 2029, in each case subject to the approval of the Board, equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the calendar month before the date of the automatic increase and (ii) 360,000 shares; provided that prior to the date of any such increase, the Board may determine that such increase will be less than the amount set forth in clauses (i) and (ii). As of December 31, 2019, no shares of common stock had been issued under the ESPP. The first offering period has not yet been decided by the Board.

9. STOCKHOLDERS’ EQUITY

As of December 31, 2019, the authorized capital stock of the Company consists of 100,000,000 shares of common stock, par value $0.0001 per share. As of December 31, 2018, the authorized capital stock of the Company consists of 20,441,982 shares of common stock, par value $0.0001 per share, and 10,883,950 shares of convertible preferred stock, par value $0.0001 per share, of which 3,093,898 are designated as Series A convertible preferred stock (“Series A Preferred Stock”) and 7,790,052 are designated as Series B Preferred Stock (collectively, with the Series A Preferred Stock, the “Preferred Stock”).

Common Stock

Voting

The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of the stockholders. There is no cumulative voting.

Preferred Stock

In January 2017, the Company issued 3,093,898 shares of Series A Preferred Stock at $2.26 per share for gross proceeds of $7.0 million. Issuance costs were $0.7 million, which included the issuance of warrants to purchase common stock (see Note 7).

Between November and December 2018, the Company issued an aggregate of 2,904,127 shares of its Series B Preferred Stock at $7.49 per share for gross proceeds of $21.7 million. Issuance costs were $0.8 million, which included the obligation to issue warrants to purchase common stock (see Note 7). In addition, all of the outstanding principal and accrued interest under the 2018 Notes were automatically converted into an aggregate of 1,097,721 shares of its Series B Preferred Stock.

In February 2019, the Company issued 442,925 shares of Series B Preferred Stock at $7.49 per share for gross proceeds of approximately $3.3 million. Issuance costs were $0.3 million, which included the obligation to issue warrants to purchase common stock (see Note 9).

As of December 31, 2019 and 2018, Preferred Stock consisted of the following (in thousands, except share data):

	December 31, 2019				
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Value	Common Stock Issuable Upon Conversion
Series A Preferred Stock	—	—	$ —	$ —	—
Series B Preferred Stock	—	—	—	$ —	—
	—	—	$ —	$ —	—

	December 31, 2018				
	Preferred Stock Authorized	Preferred Stock Issued and Outstanding	Carrying Value	Liquidation Value	Common stock Issuable Upon Conversion
Series A Preferred Stock	3,093,898	3,093,898	$ 6,254	$ 7,000	3,093,898
Series B Preferred Stock	7,790,052	4,001,848	29,156	29,964	4,001,848
	10,883,950	7,095,746	$ 35,410	$ 36,964	7,095,746

The following is a summary of the rights and privileges of the common and preferred stockholders as of December 31, 2018:

Voting

The holders of Preferred Stock have the right to one vote for each share of common stock into which such Preferred Stock could be converted and will vote together with the holders of common stock as a single class.

Dividends

Dividends are payable to holders of Preferred Stock prior to payment of any dividend to holders of common stock. Dividends are payable when and if declared out of funds legally available and such dividends are not cumulative. In the event the board of directors of the Company declares a dividend payable on the common stock, the holders of the Preferred Stock would be entitled to receive the amount of dividends per share of Preferred Stock that would be payable on the number of whole shares of the common stock into which each share of such Preferred Stock held by each holder could be converted into.

Liquidation

In the event of any liquidation, dissolution or winding up of the Company, or a Deemed Liquidation Event (as defined below), the holders of shares of Preferred Stock then outstanding are entitled to be paid out of the assets of the Company available for distribution to its stockholders before any payment shall be made to the holders of common stock by reason of their ownership thereof, in an amount per share equal to the greater of (i) the original issue price ($2.26 per share for Series A Preferred Stock and $7.49 per share for Series B Preferred Stock) plus any dividends declared but unpaid thereon or (ii) such amount per share as would have been payable had each series of Preferred Stock been converted into common stock immediately prior to a liquidation, dissolution or winding up of the Company or Deemed Liquidation Event. If upon any such liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, the proceeds shall be insufficient to pay the holders of shares of Preferred Stock the full amount to which they shall be entitled, the holders of shares of Preferred Stock shall share ratably in any distribution of the proceeds in proportion to the respective amounts which would otherwise be payable in respect of the shares of Preferred Stock held by them upon such distribution if all amounts payable with respect to such shares were paid in full. After the payment of all preferential amounts to be paid to the holders of shares of Preferred Stock, the remaining proceeds shall be distributed among the holders of shares of common stock pro rata based on the number of shares held by each such holder.

A Deemed Liquidation Event is defined as: (i) a merger where the Company is a constituent party or a subsidiary of the Company is a constituent party and the Company issues shares of its capital stock pursuant to such merger or consolidation, except any such merger or consolidation involving the Company or a subsidiary in which the shares of capital stock of the Company outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, at least a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation; or (ii) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Company or any subsidiary of the Company of all or substantially all the assets of the Company and its subsidiaries taken as a whole, or the sale or disposition (whether by merger or otherwise) of one or more subsidiaries of the Company if substantially all of the assets of the Company and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Company.

Protective Provisions

At any time when any shares of Preferred Stock remain outstanding, the Company shall not take any of the following actions without the vote or written consent of the holders of a majority of the then outstanding shares of Preferred Stock separately as a class: (i) liquidate, dissolve or wind-up the business and affairs of the Company, effect any merger, consolidation or any other Deemed Liquidation Event, or consent to any of the foregoing, in each case other than in the event that such event would provide the holders of the Preferred Stock a return per each share of Preferred Stock, including all distributions and dividends paid to such holders prior to such event by the Company, if any, of at least two (2) times the Series B Original Issue Price in the twenty-four (24) months following the Series B Original Issue Date (November 5, 2018) or three (3) times the Series B Original Issue Price thereafter; (ii) amend, alter, or repeal any provision of the Certificate of Incorporation or the Company’s bylaws in a manner that adversely affects the powers, preferences or rights of the Preferred Stock; (iii) create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of capital stock unless the same ranks junior to the Preferred Stock with respect

to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends and rights of redemption, or increase the authorized number of shares of Preferred Stock; (iv) purchase or redeem (or permit any subsidiary to purchase or redeem) or pay or declare any dividend or make any distribution on, any shares of capital stock of the Company other than (a) redemptions of or dividends or distributions on the Preferred Stock as expressly authorized herein, (b) dividends or other distributions payable on the common stock solely in the form of additional shares of common stock and (c) repurchases of stock from former employees, officers, directors, consultants or other persons who performed services for the Company or any subsidiary in connection with the cessation of such employment or service at the lower of the original purchase price or the then-current fair market value thereof; (v) create, or authorize the creation of, or issue, or authorize the issuance of any debt security, or permit any subsidiary to take any such action with respect to any debt security, if the aggregate indebtedness of the Company and its subsidiaries for borrowed money following such action would exceed $2.0 million other than equipment leases or bank lines of credit; (vi) create, or hold capital stock in, any subsidiary that is not wholly owned (either directly or through one or more other subsidiaries) by the Company, or sell, transfer or otherwise dispose of any capital stock of any direct or indirect subsidiary of the Company, or permit any direct or indirect subsidiary to sell, lease, transfer, exclusively license or otherwise dispose (in a single transaction or series of related transactions) of all or substantially all of the assets of such subsidiary; or (vi) increase or decrease the authorized number of directors of the Company.

Optional Conversion Rights

Each share of Preferred Stock is convertible, at the option of the holder thereof, at any time and from time to time after issuance, and without the payment of additional consideration into such number of fully paid and nonassessable shares of common stock as is determined by dividing the original issue price ($2.26 per share for Series A Preferred Stock and $7.49 per share for Series B Preferred Stock) by the series conversion price ($2.26 per share for Series A Preferred Stock and $7.49 per share for Series B Preferred Stock) in effect at the time of conversion. As of December 31, 2018, the Preferred Stock is convertible in to common stock on a one-for-one basis.

Mandatory Conversion Rights

All outstanding shares of Preferred Stock shall automatically be converted into shares of common stock, at the then effective conversion rate, upon either (a) the closing of the sale of shares of common stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $30.0 million of proceeds, net of the underwriting discount and commissions, to the Company, or (b) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of at least a majority of the then outstanding shares of Preferred Stock.

Redemption

The Preferred Stock is redeemable upon the occurrence of a Deemed Liquidation Event, which is not solely in control of the Company. Therefore, the Preferred Stock has been classified as temporary equity.

10. WARRANTS

Warrants Issued with Series A Preferred Stock

On January 26, 2017, in connection with the sale and issuance of the Series A Preferred Stock, the Company issued equity-classified warrants to purchase 309,389 shares of common stock (the “2017 Warrants”), valued at $0.2 million, and included in the issuance costs of the Series A Preferred Stock (see Note 4). The warrants vested immediately and have an exercise price of $2.49 per share and expire on March 13, 2027.

The fair value of warrants issued is estimated using the Black-Scholes option pricing model with the following assumptions for the 2017 Warrants.

Contractual term (in years)	10.0
Volatility	74.48 %
Risk-free interest rate	3.20 %
Dividend yield	0.00 %

On December 5, 2019, an optionholder exercised 20,000 options in a cashless exercise at net, and the Company issued 17,026 shares of common stock.

Warrants Issued with the 2018 Notes

On January 18, 2018, the Company entered into a placement agent agreement through which it became obligated to issue common stock warrants in connection with the issuance of the 2018 Notes. The obligation to issue the 2018 Notes Warrants was recorded as a liability at its fair value (see Note 3), which was initially $0.1 million, and was included in the issuance costs of the 2018 Notes (see Note 4). On November 5, 2018, in connection with the extinguishment of the 2018 Notes into shares of Series B Preferred Stock, the Company issued the 2018 Notes Warrants, which were equity-classified warrants upon issuance, to purchase 76,847 shares of common stock, valued at $0.3 million. The 2018 Notes Warrants vested immediately upon issuance and have an exercise price of $6.59 per share and expire on November 4, 2028.

Warrants Issued with Series B Preferred Stock

In November and December 2018, in connection with the sale and issuance of the Series B Preferred Stock, the Company was obligated to issue equity-classified warrants to purchase 72,261 shares of common stock (collectively the “2018 Warrants”), valued in the aggregate at $0.2 million, which was included in the issuance costs for the Series B Preferred Stock (see Note 6). The warrants vest immediately upon issuance, have an exercise price of $8.24 per share and expire 10 years from the date of issuance.

The fair value of the 2018 Warrants is estimated using the Black-Scholes option pricing model with the following assumptions:

Contractual term (in years)	10.0
Volatility	73.22 %
Risk-free interest rate	2.70 %
Dividend yield	0.00 %

A summary of the Company’s outstanding common stock warrants as of December 31, 2019 is as follows:

	Warrants
Outstanding as of December 31, 2018	386,236
Warrants granted and issued	96,128
Warrants exercised	(20,000)
Warrants exchanged	—
Balance as of December 31, 2019	462,364

11. LEASES

The following table summarizes our lease assets and liabilities as of December 31, 2019:

ROU Assets and Liabilities	Balance Sheet Location	Operating
ROU - Asset	Right-of-use assets	$ 2,035
Lease liabilities (current)	Operating lease liabilities, current	356
Lease liabilities (non-current)	Operating lease liabilities, non-current	1,683

The following table summarizes our lease related costs for the twelve months ended December 31, 2019:

Lease Cost	Statement of Operations Location	Operating
Operating Lease Cost	General and administrative	$ 81
Total Lease Cost		$ 81

Average lease terms and discount rates for the Company's operating leases were as follows:

Other Information	Year Ended December 31, 2019
Weighted-average remaining lease term	
Operating leases	4.8 years
Weighted-average discount rate	
Operating leases	5.69%

The following table summarizes the maturities of lease liabilities as of December 31, 2019:

Year	Operating
2020	$ 462
2021	474
2022	486
2023	497
2024	424
Thereafter	—
Total lease payments	2,343
Less: interest	304
Total lease liabilities	$ 2,039

12. INCOME TAXES

The Company's current tax provision for the years ended December 31, 2019 and 2018 is $0 and $0, respectively. The Company's deferred tax provision for the years ended December 31, 2019 and 2018 is $0 and $0, respectively.

Deferred income tax assets and liabilities consist of the following (in thousands):

	Year ended December 31,	
	2019	2018
Deferred tax assets/(liabilities)		
Accrued expenses	$ —	$ —
Operating lease liability	706	—
Stock-based compensation	1,582	98
Capitalized startup costs	22	35
Right of use asset	(705)	—
Net operating losses	19,937	6,176
Total deferred tax assets	21,542	6,309
Less: valuation allowance	(21,542)	(6,309)
Net deferred tax asset (liability)	$ —	$ —

Deferred tax assets result primarily from unutilized net operating losses, stock-based compensation, operating lease liability, and timing differences as a result of the Company reporting its income tax returns. As of December 31, 2019, the Company had approximately $57.6 million of federal operating losses (“NOLs”) carried forward. Of this amount, approximately $3.6 million will begin to expire in 2037 and approximately $54.0 million are carried forward indefinitely. The Company had approximately $57.6 million in state net operating loss carryforwards available to offset future taxable income. Some of these net operating losses follow the Federal Tax Cuts and Jobs Act and are indefinite life and other are definite life with various expiration dates. Additionally, the Company generated approximately $39.8 million of NOLs in 2019 which, for federal income tax purposes, do not expire but are limited to offsetting up to 80% of future taxable income.

The NOL carry forwards are subject to review and possible adjustment by the U.S. and state tax authorities. NOL carry forwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Sections 382 Internal Revenue Code. This could limit the amount of NOLs that the Company can utilize annually to offset future taxable income or tax liabilities. As of December 31, 2019, the Company has not performed such an analysis. Subsequent ownership changes and proposed future changes to tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years.

In assessing the realizability of the Company’s deferred tax assets, management considers whether or not it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income. The Company’s assessment is based on the weight of available evidence, including cumulative losses since inception and expected future losses and, as such, the Company does not believe it is more likely than not that the deferred tax assets will be realized. Accordingly, a full valuation allowance has been established and no deferred tax assets and related tax benefit have been recognized in the accompanying financial statements. At December 31, 2019 and 2018, the Company recorded valuation allowances of $21.5 million and $6.3 million, respectively, representing an increase in the valuation allowance of $15.3 million in 2019 due to the uncertainty regarding the realization of such deferred tax assets, to offset the benefits of net operating losses generated during those years.

The U.S. federal statutory corporate tax rate reconciles to the Company's effective tax rate for the years ended December 31, 2019 and 2018:

	Year Ended December 31,	
	2019	2018
Federal statutory rate	21.0 %	21.0 %
State and local taxes net of federal tax benefit	13.2	13.5
Tax rate change	0.0	0.3
Change in valuation allowance	(33.4)	(28.5)
Permanently disallowed interest expense	(0.7)	(6.3)
Other	(0.1)	—
Total	0.0 %	0.0 %

13. BENEFIT PLANS

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code in 2018. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the plan may be made at the discretion of the Company's board of directors. The Company made approximately $69,000 and $11,000 in matching contributions to the plan during the year ended December 31, 2019 and 2018, respectively.

14. NET LOSS PER COMMON SHARE

Basic net loss per common share is computed by dividing the net loss available to common stockholders by the weighted-average number of shares of common stock outstanding during the period.

Diluted net loss per common share is computed by giving the effect of all potential shares of common stock, including stock options, preferred shares, warrants and instruments convertible into common stock, to the extent dilutive. Basic and diluted net loss per common share was the same for the years ended December 2019 and 2018, as the inclusion of all potential common shares outstanding would have been anti-dilutive.

The following table sets forth the computation of basic and diluted net loss per common share (in thousands, except share and per share data):

	Years Ended December 31,	
	2019	2018
Numerator:		
Net loss	$ (45,513)	$ (16,521)
Denominator:		
Weighted-average common stock outstanding	12,831,221	5,483,149
Net loss per share attributable to common stockholders - basic and diluted	$ (3.55)	$ (3.01)

The Company's potential dilutive securities, which include Preferred Stock, stock options and warrants, have been excluded from the computation of diluted net loss per share as the effect would be to reduce the net loss per share. Therefore, the weighted-average number of common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The Company excluded the following potential common

shares, presented based on amounts outstanding at December 31, 2019 and 2018, from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	As of December 31,	
	2019	2018
Preferred Stock	—	3,093,898
Options to purchase common stock	4,079,888	1,035,466
Warrants to purchase common stock	462,364	309,389

15. RELATED PARTIES

In December 2018, the Company entered into an agreement (the "LaunchLabs Agreement") with ARE-LaunchLabs NYC LLC ("Alexandria LaunchLabs"), a subsidiary of Alexandria Real Estate Equities, Inc. for use of specified premises within the Alexandria LaunchLabs space. A member of the Company's board of directors is the founder and executive chairman of Alexandria Real Estate Equities, Inc. During the years ended December 31, 2019 and 2018, the Company made payments to Alexandria LaunchLabs of approximately $85,000 and $13,000, respectively under the LaunchLabs Agreement, which was recognized in research and development expenses. As of December 31, 2019, there were no amounts due to Alexandria LaunchLabs under the LaunchLabs Agreement.

16. SUBSEQUENT EVENTS

On January 28, 2020, the Company completed a public offering of 3,152,712 shares of common stock. The offering consisted of 3,152,712 shares of common stock, including the exercise in full of the underwriters' option to purchase 411,223 additional shares of common stock. The shares were offered at a price to the public of $45.50 per share, resulting in aggregate gross proceeds of approximately $143.4 million, before deducting underwriting discounts and commissions and estimated offering expenses.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Evaluation of Controls and Procedures

As of December 31, 2019, our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, evaluated the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that, as of December 31, 2019, the design and operation of our disclosure controls and procedures were effective at the reasonable assurance level.

Management’s Annual Report on Internal Control over Financial Reporting

This annual report does not include a report of management’s assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the fourth quarter of 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

Shendelman Employment Agreement

The Company entered into an employment agreement with Dr. Shoshana Shendelman, the Company’s Chief Executive Officer, on March 9, 2020.

The employment agreement with Dr. Shendelman provides that she will receive an annual base salary of $577,500 and will be eligible to receive an annual performance and retention bonus of up to 50% of her annual base salary. The employment agreement with Dr. Shendelman further provides that she (or her estate, as applicable) will be eligible to receive certain severance payments and benefits upon a qualifying termination of her employment by the Company without “ cause” (including as a result of her death or disability) or by Dr. Shendelman for “ good reason” (in each case as such terms are defined in Dr. Shendelman’s employment agreement), subject to her (or her estate’s, as applicable) execution of a release of claims in favor of the Company. The severance payments and benefits consist of (1) 12 months of base salary continuation, (2) a lump sum target annual bonus payment, (3) continued payment for the cost of health care coverage for 12 months and (4) accelerated vesting of any then-unvested shares subject to an outstanding option.

Dr. Shendelman’s employment agreement further provides that, notwithstanding anything in her employment agreement, any equity plan of the Company or any award agreement to the contrary, in the event of a “ change in

control” (as defined in the Company’s 2019 Equity Incentive Plan), Dr. Shendelman’s then-unvested outstanding equity awards will become fully vested (and exercisable, as applicable) as of the date of such change in control.

The foregoing description of the terms of the employment agreement with Dr. Shendelman is a summary of certain of its terms only and is qualified in its entirety by the full text of the agreements filed as Exhibit 10.16 hereto and incorporated herein by reference.

Perfetti Employment Agreement Amendment

As previously disclosed, the Company entered into an employment agreement with Dr. Riccardo Perfetti, the Company’s Chief Medical Officer, on August 28, 2019 (the “Perfetti Employment Agreement”). On March 9, 2020, the Perfetti Employment Agreement was amended to provide that (i) a termination of his employment due to death or disability shall constitute a “ qualifying termination” (as defined in the Perfetti Employment Agreement) and (ii) notwithstanding anything in the Perfetti Employment Agreement, any equity plan of the Company or any award agreement to the contrary, in the event of a “ change in control” (as defined in the Company’s 2019 Equity Incentive Plan), Dr. Perfetti’s then-unvested outstanding equity awards will become fully vested (and exercisable, as applicable) as of the date of such change in control.

The foregoing description of the terms of the amendment to the Perfetti Employment Agreement is a summary of certain of its terms only and is qualified in its entirety by the full text of the amendment to the Perfetti Employment Agreement filed as Exhibit 10.17 hereto and incorporated herein by reference.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The information required by this item with respect to our executive officers is provided under the caption entitled "Information about our Executive Officers" in Part I of this Annual Report on Form 10-K and is incorporated by reference herein. Other information required by this item will be set forth in our definitive Proxy Statement under the captions "General Information About the Board of Directors," "Election of Directors," and "Code of Ethics" to be filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference to our Proxy Statement.

The following table sets forth information regarding our directors, including their ages as of December 31, 2019:

Name	Age	Position(s)
Directors		
Shoshana Shendelman, Ph.D. (3)	41	President, Chief Executive Officer and Chair of the Board of Directors
Les Funtleyder	50	Director
Stacy J. Kanter (1) (3)	61	Director
Teena Lerner, Ph.D. (1) (2)	62	Director
Joel S. Marcus (1) (2)	72	Director
Jay S. Skyler, M.D., MACP (2) (3)	72	Director

(1) Member of our audit committee.

(2) Member of our compensation committee.

(3) Member of our nominating and corporate governance committee.

Directors

Les Funtleyder has served as a member of our board of directors since June 2016 and previously served as our interim Chief Financial Officer from December 2018 to April 2019. Mr. Funtleyder also serves as a healthcare portfolio manager at E Squared Capital Management, LLC since January 2014, a senior external advisor with McKinsey and Co. since June 2017, and a consulting partner at Bluecloud Health, a private equity healthcare fund, since December 2013. Mr. Funtleyder previously served as the director of strategic investments and communications of OPKO Health Inc., a publicly traded healthcare company. Mr. Funtleyder currently serves on the board of directors of several private healthcare companies and foundations. Mr. Funtleyder is also an adjunct professor at Columbia University Medical Center. Mr. Funtleyder received his B.A. from Tulane University and MPH from Columbia University Mailman School of Public Health. We believe that Mr. Funtleyder's extensive experience managing and investing in the healthcare industry qualifies him to serve on our board of directors.

Stacy J. Kanter has served as a member of our board of directors since May 2019. Ms. Kanter practiced law for more than 30 years with Skadden, Arps, Slate, Meagher & Flom LLP, where she was a partner from 1993 until December 2018 and Head of the Global Capital Markets practice from 2009 until December 2018 and was Of Counsel from January 2019 until joining our board of directors. Ms. Kanter also chaired Skadden's Global Diversity and Inclusion Committee. Ms. Kanter was an associate at Skadden from 1984 to 1986 and from 1988 to 1993. Ms. Kanter served as a law clerk to the Honorable Raymond J. Dearie, United States District Court Judge for the Eastern District of

New York from 1986 to 1987. Ms. Kanter received her B.S. in Business Administration and Management from the University at Albany School of Business and her J.D. from Brooklyn Law School. We believe that Ms. Kanter's extensive legal and business expertise in corporate finance and capital markets, corporate governance and mergers and acquisitions qualifies her to serve on our board of directors.

Teena Lerner, Ph.D., has served as a member of our board of directors since March 2017. Dr. Lerner has served on the Technology Transfer Advisory Committee of The Rockefeller University since 2000. In 2002, Dr. Lerner founded Rx Capital Management LP, a healthcare equity hedge fund, and served as the Chief Executive Officer until 2006. Prior to that, she was a portfolio manager at Pequot Capital Management, Inc., an investment advisory firm, and served as a Managing Director, Equity Research at Lehman Brothers Holdings Inc., a global financial services firm. Dr. Lerner received a B.S. from City University of New York-Brooklyn College, an MBA from New York University, Stern School of Business, a Ph.D. in Molecular Biology/Retrovirology from The Rockefeller University and a CFA charter from the Institute of Chartered Financial Analysts. We believe that Dr. Lerner's extensive expertise in various areas of the healthcare industry, including as investment banking and research, qualifies her to serve on our board of directors.

Joel S. Marcus has served as a member of our board of directors since January 2017. Mr. Marcus founded Alexandria Real Estate Equities, Inc., or Alexandria Real Estate, a publicly traded real estate investment trust, and currently serves as Executive Chairman after previously serving as its Chairman since May 2007, Chief Executive Officer since March 1997 and a director since its founding in 1994. Mr. Marcus also co-founded and leads Alexandria Venture Investments, LLC, a strategic venture arm of Alexandria Real Estate. Prior to founding Alexandria Real Estate, Mr. Marcus had an extensive legal career specializing in corporate finance and capital markets, venture capital and mergers and acquisitions with special expertise in the biopharmaceutical industry. Mr. Marcus currently serves on the boards of directors of Intra-Cellular Therapies, Inc. and MeiraGTx Holdings plc, each a publicly traded biopharmaceutical company, as well as Atara Biotherapeutics, Inc., a publicly traded immunotherapy company. He also serves on the boards of directors of several private companies. Mr. Marcus received both his B.A. and J.D. from the University of California, Los Angeles. We believe that Mr. Marcus' extensive experience in the life sciences industry and as a chief executive officer and attorney qualifies him to serve on our board of directors.

Jay S. Skyler, M.D., MACP has served on our board of directors since April 2019. Dr. Skyler is a Professor of Medicine, Pediatrics and Psychology and Deputy Director of the Diabetes Research Institute at the University of Miami in Florida, where he has been employed since 1976. Dr. Skyler has also served as Study Chairman for the National Institute of Diabetes & Digestive & Kidney Diseases Type 1 Diabetes clinical trials network. He was previously the President of the American Diabetes Association and Vice-President of the International Diabetes Federation. Dr. Skyler served as a director of Amylin Pharmaceuticals, Inc., a pharmaceutical company, until its acquisition by Bristol-Myers Squibb Company in August 2012, and served as a director of MiniMed, Inc., a medical device company, until its acquisition by Medtronic plc. in 2001. Dr. Skyler currently serves on the board of directors of DexCom, Inc., a publicly traded medical device company. He also serves on the boards of directors of several private companies. Dr. Skyler received a B.S. from Pennsylvania State University and an M.D. from Jefferson Medical College. We believe that Dr. Skyler's extensive expertise in the life sciences industry and his experience serving on the board of directors of a public company qualifies him to serve on our board of directors.

Director Independence

Under The Nasdaq Stock Market LLC, or Nasdaq, Marketplace Rules, or the Nasdaq Listing Rules, independent directors must comprise a majority of our board of directors as a public company within one year of listing.

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that none of our directors except Shoshana Shendelman, representing one of our six directors, will have any relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under the applicable rules and regulations of the SEC and the listing requirements of the Nasdaq Listing Rules. Our board of directors has determined that Dr. Shendelman, by virtue

of her position as our President and Chief Executive Officer, is not independent under applicable rules and regulations of the SEC and the Nasdaq Listing Rules. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and in the case of Mr. Funtleyder, the fact that he was our former Interim Chief Financial Officer.

Board Composition

Our board of directors currently consists of six members. In accordance with our amended and restated certificate of incorporation our board of directors is divided into three classes with staggered three-year terms. At each annual general meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Our directors are divided among the three classes as follows:

- the Class I directors are Les Funtleyder and Stacy J. Kanter, and their terms will expire at the annual meeting of stockholders to be held in 2020;
- the Class II directors are Jay Skyler, M.D. and Joel S. Marcus, and their terms will expire at the annual meeting of stockholders to be held in 2021; and
- the Class III directors are Shoshana Shendelman, Ph.D. and Teena Lerner, Ph.D., and their terms will expire at the annual meeting of stockholders to be held in 2022.

We expect that any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business. The composition and functions of each committee are described below. Members serve on these committees until their resignation or until otherwise determined by our board of directors. Each committee has adopted a written charter that satisfies the applicable rules and regulations of the SEC and Nasdaq Listing Rules, which we have posted on our website at www.appliedtherapeutics.com.

Audit Committee

The audit committee is responsible for assisting our board of directors in its oversight of the integrity of our financial statements, the qualifications and independence of our independent auditors and our internal financial and accounting controls. The audit committee has direct responsibility for the appointment, compensation, retention (including termination) and oversight of our independent auditors, and our independent auditors report directly to the audit committee. The audit committee also prepares the audit committee report that the SEC requires to be included in our annual proxy statement.

Our audit committee consists of Teena Lerner, Ph.D., Joel S. Marcus and Stacy J. Kanter. Our board of directors has determined that all three members are independent under the Nasdaq Listing Rules and Rule 10A-3(b)(1) of the Exchange Act. The chair of our audit committee is Ms. Kanter. Our board of directors has determined that Dr. Lerner and Mr. Marcus are each an “ audit committee financial expert” as such term is currently defined in Item 407(d)(5) of Regulation S-K. Our board of directors has also determined that each member of our audit committee can read and understand fundamental financial statements, in accordance with applicable requirements. In arriving at these

determinations, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

Compensation Committee

The compensation committee approves the compensation objectives for the company, the compensation of the chief executive officer and approves, or recommends to our board of directors for approval, the compensation for other executives. The compensation committee reviews all compensation components, including base salary, bonus, and benefits.

Our compensation committee consists of Teena Lerner, Ph.D., Joel S. Marcus and Jay S. Skyler, M.D. Our board of directors has determined that all members are independent under the Nasdaq Listing Rules and are "nonemployee directors" as defined in Rule 16b-3 promulgated under the Exchange Act. The chair of our compensation committee is Dr. Lerner.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee makes recommendations regarding corporate governance, the composition of our board of directors, identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. In addition, the nominating and corporate governance committee is responsible for developing and recommending corporate governance guidelines to our board of directors, as applicable to the company.

Our nominating and corporate governance committee consists of Shoshana Shendelman, Ph.D., Jay S. Skyler, M.D. and Stacy J. Kanter. The chair of our nominating and corporate governance committee is Dr. Skyler. Each member of the nominating and corporate governance committee is a non-employee director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act, an independent director as defined by the Nasdaq Listing Rules and is free from any relationship that would interfere with the exercise of his or her independent judgment, as determined by the board of directors in accordance with the applicable Nasdaq Listing Rules.

Compensation Committee Interlocks and Insider Participation

None of the members of the compensation committee is currently, or has been at any time, one of our executive officers or employees. None of our executive officers currently serves, or has served during the last year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or on our compensation committee.

ITEM 11. EXECUTIVE AND DIRECTOR COMPENSATION.

Our named executive officers for the year ended December 31, 2019, consisting of our principal executive officer and our two other executive officers who were serving as of December 31, 2019, are as follows:

- Shoshana Shendelman, Ph.D., our President and Chief Executive Officer;
- Mark Vignola, Ph.D., our Chief Financial Officer; and
- Riccardo Perfetti, M.D., Ph.D., our Chief Medical Officer.

Summary Compensation Table

The following table provides information regarding the compensation earned by our named executive officers for the year ended December 31, 2019.

Name and Principal Position	Year	Salary ($)[1]	Bonus ($)	Option Awards ($)[2]	All Other Compensation ($)[3]	Total ($)
Shoshana Shendelman, Ph.D.	2019	550,000	—	11,039,972 [4]	—	11,589,972
President and Chief Executive Officer	2018	500,000	—	685,554	—	1,185,554
Mark Vignola, Ph.D.	2019	400,000	160,000	1,508,882	8,151	2,077,033
Chief Financial Officer						
Riccardo Perfetti, M.D., Ph.D.	2019	450,000	297,500 [5]	2,600,221 [7]	9,594	3,357,315
Chief Medical Officer	2018	167,307	275,000 [6]	725,241	10,221	1,177,769

(1) Salary amounts represent actual amounts paid during the applicable year. See "—Narrative to the Summary Compensation Table—Annual Base Salary" below for more information.

(2) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during the applicable year computed in accordance with ASC 718 for stock-based compensation transactions. Assumptions used in the calculation of these amounts are included in the notes to our financial statements included elsewhere in this Annual Report. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(3) The amounts represent matching contributions made by us to the named executive officer's 401(k) plan account.

(4) Consists of (i) an annual grant of options made on March 18, 2019 in respect of 2018 performance, (ii) an IPO grant of options granted on May 13, 2019, (iii) a grant of options made on December 16, 2019 in respect of 2019 performance in lieu of a grant of options that would have otherwise been made in early 2020 in respect of 2019 performance and (iv) a fully vested grant of options made on December 16, 2019 in lieu of an annual cash bonus in respect of 2019. While certain of these options relate to 2018 performance and certain others relate to 2019 performance, the applicable compensation disclosure rules require that the value of all of the option grants be included in this table.

(5) Consists of Dr. Perfetti's retention bonus ($50,000) and an annual discretionary bonus for the 2019 calendar year ($247,500)..

(6) Consists of Dr. Perfetti's sign-on bonus ($50,000) and an annual discretionary bonus for the 2018 calendar year ($225,000).

(7) Consists of the following option awards to Dr. Perfetti: (i) an annual grant of options made on March 18, 2019 in respect of 2018 performance, (ii) an IPO grant of options made on May 13, 2019 and (iii) a grant of options made on December 16, 2019 in respect of 2019 performance in lieu of a grant of options that would have otherwise been made in early 2020 in respect of 2019 performance. While certain of these options relate to 2018 performance and certain others relate to 2019 performance, the applicable compensation disclosure rules require that the value of all of the option grants be included in this table.

Narrative to the Summary Compensation Table

We review compensation annually for all employees, including our named executive officers. In setting executive base salaries and bonuses and granting equity incentive awards, we consider compensation for comparable positions in the market, the historical compensation levels of our executives, individual performance as compared to our

expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders and a long-term commitment to our company.

Prior to the completion of the IPO, our board of directors determined our executive officers' compensation and reviewed and discussed management's proposed compensation with our chief executive officer for all executives other than our chief executive officer. Based on those discussions and its discretion, our board of directors then approved the compensation of each executive officer. Since the completion of the IPO, the compensation committee has determined our executive officers' compensation and followed this process, but the compensation committee itself, rather than our board of directors, approves the compensation of each executive officer.

Annual Base Salary

Base salaries for our executive officers are initially established through arm's-length negotiations at the time of the executive officer's hiring, taking into account such executive officer's qualifications, experience, the scope of his or her responsibilities and competitive market compensation paid by other companies for similar positions within the industry and geography. Base salaries are reviewed annually, typically in connection with our annual performance review process, and adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. In making decisions regarding salary increases, we may also draw upon the experience of members of our board of directors with executives at other companies. The 2019 base salaries for our named executive officers were as follows: (a) $550,000 for Dr. Shendelman, (b) $450,000 for Dr. Perfetti and (c) $400,000 for Dr. Vignola.

Bonus

Our named executive officers are eligible to receive discretionary annual bonuses based on individual performance, company performance or as otherwise determined appropriate by our compensation committee. In late 2019, the compensation committee met and, after considering input from management and considering relevant company and individual performance, determined to award the following annual bonuses to our named executive officers in respect of 2019: (a) a bonus in the form of a grant of fully vested options to purchase 23,317 shares of our common stock, which was granted to Dr. Shendelman in lieu of a cash bonus, (b) a cash bonus of $160,000 to Dr. Vignola and (c) a cash bonus of $247,500 to Dr. Perfetti.

Stock Option Grants

Our equity-based incentive awards are designed to align our interests and those of our stockholders with those of our employees and consultants, including our named executive officers. As of December 31, 2019, stock option awards were the only form of equity awards we granted to our named executive officers.

We have historically used stock options as an incentive for long-term compensation to our named executive officers because they are able to profit from stock options only if our stock price increases relative to the stock option's exercise price, which exercise price is set at the fair market value of our common stock on the date of grant. We may grant equity awards at such times as our board of directors determines appropriate. Additional grants may occur periodically in order to specifically incentivize executives with respect to achieving certain corporate goals or to reward executives for exceptional performance.

Prior to the IPO, all of the stock options we granted were made pursuant to the 2016 Plan. Following the IPO, our equity incentive awards were granted under the terms of the 2019 Plan. The terms of our equity plans are described below under "—Equity Incentive Plans."

All options are granted with an exercise price per share that is no less than the fair market value of our common stock on the date of grant of such award. Our stock option awards generally vest over a three-year period, and may be subject to acceleration of vesting and exercisability under certain termination and change in control events. See "—Outstanding Equity Awards at Fiscal Year-End" below for additional information.

Outstanding Equity Awards at Fiscal Year-End

The following table provides information regarding the outstanding equity awards held by our named executive officers as of December 31, 2019.

		Option Awards			
Name and Principal Position	Grant Date	Number of Securities Underlying Unexercised Options (#) (Exercisable)	Number of Securities Underlying Unexercised Options (#) (Unexercisable)	Option Exercise Price ($)	Option Expiration Date
Shoshana Shendelman, Ph.D.					
President and Chief Executive Officer	March 21, 2017 [1]	27,624	—	1.00	March 21, 2027
	March 8, 2018 [2]	484,641	242,320	1.44	March 7, 2028
	March 18, 2019 [3]	316,298	632,596	4.70	March 17, 2029
	May 13, 2019 [4]	—	767,349	10.00	May 13, 2029
	December 16, 2019 [5]	—	209,000	22.20	December 16, 2029
	December 16, 2019 [1]	23,317	—	22.20	December 16, 2029
Mark Vignola					
Chief Financial Officer	May 3, 2019 [6]	—	161,594	12.93	May 3, 2029
	May 13, 2019 [4]	—	34,104	10.00	May 13, 2029
Riccardo Perfetti, M.D., Ph.D.					
Chief Medical Officer	December 17, 2018 [7]	165,996	47,428	1.44	December 16, 2028
	March 18, 2019 [8]	78,057	55,755	4.70	March 17, 2029
	May 13, 2019 [4]	—	170,522	10.00	May 13, 2029
	December 16, 2019 [5]	—	80,000	22.20	December 16, 2029

(1) This option was fully vested as of December 31, 2019.

(2) Two-thirds of this option was vested as of December 31, 2019, and the remainder will vest on March 8, 2020.

(3) One-third of this option was vested as of December 31, 2019, and the remainder will vest on each of March 18, 2020 and March 8, 2021.

(4) One-fourth of this option vests on May 13, 2020, and the remainder vests monthly thereafter in one thirty-sixth increments.

(5) One-fourth of this option vests on December 16, 2020, and the remainder vests monthly thereafter in one thirty-sixth increments.

(6) One-third of this option vests on April 27, 2020, and the remainder vests monthly in one twenty-fourth increments.

(7) One-third of this option vested on August 27, 2018, an additional sixteen twenty-fourths was vested as of December 31, 2019 and the remainder vests monthly in one twenty-fourth increments.

(8) One-third of this option vested on March 18, 2019, an additional nine twenty-fourths was vested as of December 31, 2019 and the remainder vests monthly in one twenty-fourth increments.

IPO Option Grants

In connection with the IPO, our board of directors granted options to purchase 5% of our outstanding shares of common stock immediately following the IPO to Drs. Shendelman, Perfetti and Vignola under our 2019 Plan with an exercise price per share equal to the initial public offering price per share. One quarter of the shares underlying each of

these options vest on the first anniversary of the date of grant and the remaining shares vest in 36 equal installments thereafter, subject to the executive officer's continuous employment with us at each vesting date.

Option Grants Awarded in December 2019

Our compensation committee granted options in December 2019 to Drs. Shendelman and Perfetti in respect of their 2019 performance in lieu of grants of options that would have otherwise been made to each of them in early 2020 in respect of their 2019 performance. One quarter of the shares underlying each of these options vest on the first anniversary of the date of grant and the remaining shares vest in 36 equal installments thereafter, generally subject to the executive officer's continuous employment with us at each vesting date.

In addition, as described above in "Narrative to Summary Compensation Table — Bonus," Dr. Shendelman received a grant of fully vested options in December 2019 in lieu of payment of a cash bonus in respect of 2019 performance.

Employment Arrangements

Below are descriptions of our employment agreements with our named executive officers. The agreements generally provide for at-will employment without any specific term and set forth the named executive officer's initial base salary and eligibility for employee benefits. The key terms of the offer letters and employment agreements with our named executive officers, including potential payments upon termination or change in control, are described below. Additionally, each of Dr. Perfetti and Dr. Vignola are entitled to certain severance benefits pursuant to his agreement, the terms of which are described under "—Potential Payments and Benefits upon Termination or Change in Control" below. Each of our named executive officers has executed a form of our standard confidential information and inventions assignment agreement.

Agreement with Shoshana Shendelman

We are currently finalizing the terms of Dr. Shendelman's employment with us. Under her employment agreement, she will be entitled to an annual base salary of $550,000, which may be adjusted from time to time, will be eligible to receive an annual performance bonus and will be eligible to participate in all of the employee benefit plans that we generally make available to all of our employees. Additionally, Dr. Shendelman is expected to be entitled to certain severance benefits pursuant to her agreement, the terms of which are described under "— Potential Payments and Benefits upon Termination or Change in Control" below.

Agreement with Mark Vignola

In August 2019, we entered into an employment agreement with Dr. Vignola. Pursuant to his employment agreement, Dr. Vignola is entitled to an annual base salary of $400,000 and a discretionary annual bonus. Additionally, Dr. Vignola is entitled to certain severance benefits pursuant to his agreement, the terms of which are described under "— Potential Payments and Benefits upon Termination or Change in Control" below.

Agreement with Riccardo Perfetti

In August 2019, we entered into an employment agreement with Dr. Perfetti. Pursuant to his employment agreement, Dr. Perfetti is entitled to an annual base salary of $450,000 and a discretionary annual bonus. In addition, Dr. Perfetti received a one-time sign-on bonus of $100,000, with $50,000 payable on the first day of his employment and the remainder payable on the one-year anniversary of his start date. Additionally, Dr. Perfetti is entitled to certain severance benefits pursuant to his agreement, the terms of which are described under "— Potential Payments and Benefits upon Termination or Change in Control" below.

Potential Payments and Benefits upon Termination or Change in Control

Regardless of the manner in which a named executive officer's employment with us terminates, the named executive officer is entitled to receive amounts earned during their term of service, including salary and accrued unused vacation pay. In addition, each named executive officer is eligible for the following payments and benefits upon a qualifying termination of employment or a change in control:

Shoshana Shendelman

Dr. Shendelman's outstanding options under the 2016 Plan will vest in full upon the occurrence of a change in control, subject to her continued service through the closing of the change in control (as defined in the 2016 Plan).

It is expected that pursuant to the terms of Dr. Shendelman's proposed employment agreement, in the event of a qualifying termination, which includes an involuntary termination without "cause" and a "resignation for good reason," Dr. Shendelman will be eligible to receive at least (i) 18 months of her monthly base salary plus her target annual bonus, (ii) 18 months of payments equal to the monthly cost of her health insurance premiums at the time of termination, and (iii) accelerated vesting of any then-unvested shares subject to an outstanding option, subject to her execution of a separation agreement and general release of claims in favor of our company.

Mark Vignola

Pursuant to Dr. Vignola's employment agreement, if in the event of a qualifying termination, which includes an involuntary termination without "cause" and a "resignation for good reason," Dr. Vignola will be eligible to receive at least (i) nine months of his monthly base salary plus his target annual bonus prorated pursuant to the terms of Dr. Vignola's employment agreement, (ii) nine months of payments equal to the monthly cost of his health insurance premiums at the time of termination, and (iii) accelerated vesting of any then-unvested shares subject to an outstanding option, subject to his execution of a separation agreement and general release of claims in favor of our company.

In addition, Dr. Vignola's outstanding options under the 2016 Plan will vest in full upon the occurrence of a change in control, subject to his continued service through the closing of the change in control (as defined in the 2016 Plan).

Riccardo Perfetti

Pursuant to Dr. Perfetti's employment agreement, if in the event of a qualifying termination, which includes an involuntary termination without "cause" and a "resignation for good reason," Dr. Perfetti will be eligible to receive at least (i) 12 months of his monthly base salary plus his target annual bonus, (ii) 12 months of payments equal to the monthly cost of his health insurance premiums at the time of termination, and (iii) accelerated vesting of any then-unvested shares subject to an outstanding option, subject to his execution of a separation agreement and general release of claims in favor of our company.

In addition, Dr. Perfetti's outstanding options under the 2016 Plan will vest in full upon the occurrence of a change in control, subject to his continued service through the closing of the change in control (as defined in the 2016 Plan).

Health and Welfare and Retirement Benefits; Perquisites

All of our current named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, vision, disability and life insurance plans, in each case on the same basis as all of our other employees. We generally do not provide perquisites or personal benefits to our named executive officers, except in limited circumstances.

401(k) Plan

Our named executive officers are eligible to participate in a defined contribution retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees may defer eligible compensation on a pre-tax or after-tax (Roth) basis, up to the statutorily prescribed annual limits on contributions under the Code. Contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. We currently make matching contributions into the 401(k) plan on behalf of participants equal to 100% on participant contributions up to 3% of their compensation and 50% on participant contributions up to an additional 2% of their compensation. Participants are immediately and fully vested in their contributions. The 401(k) plan is intended to be qualified under Section 401(a) of the Code with the 401(k) plan's related trust intended to be tax-exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to the 401(k) plan (except for Roth contributions) and earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan. Our board of directors may elect to adopt qualified or nonqualified benefit plans in the future, if it determines that doing so is in our best interests.

Equity Incentive Plans

2019 Equity Incentive Plan

Our board of directors adopted our 2019 Plan on April 24, 2019 and our stockholders approved our 2019 Plan on April 26, 2019. Our 2019 Plan is a successor to and continuation of the 2016 Equity Incentive Plan, or the 2016 Plan. The 2019 Plan became effective upon, and no stock awards were granted under the 2019 Plan until, after the date of the underwriting agreement related to the IPO. Upon the 2019 Plan's effectiveness, no further grants were made under the 2016 Plan.

Stock Awards. Our 2019 Plan provides for the grant of incentive stock options, or ISOs, within the meaning of Section 422 of the Code, to employees, including employees of any parent or subsidiary, and for the grant of nonstatutory stock options, or NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other forms of stock awards to employees, directors and consultants, including employees and consultants of our affiliates.

Authorized Shares. Initially, the maximum number of shares of our common stock that may be issued under our 2019 Plan is 4,530,000 shares, which is the sum of (1) 1,618,813 new shares, plus (2) the number of shares (not to exceed 2,911,187 shares) (i) that remain available for the issuance of awards under the 2016 Plan at the time our 2019 Plan became effective, and (ii) any shares subject to outstanding stock options or other stock awards that were granted under the 2016 Plan that (A) terminate or expire prior to exercise or settlement; (B) are forfeited because of the failure to vest; or (C) are reacquired or withheld (or not issued) to satisfy a tax withholding obligation or the purchase or exercise price. In addition, the number of shares of our common stock reserved for issuance under our 2019 Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2020 through January 1, 2029, in an amount equal to 5% of the total number of shares of our capital stock outstanding on the last day of the calendar month before the date of each automatic increase, or a lesser number of shares determined by our board of directors. The maximum number of shares of our common stock that may be issued on the exercise of ISOs under our 2019 Plan is 13,000,000 shares.

Share Reserve. As of December 31, 2019, 1,749,192 shares of our common stock were reserved for issuance under the 2019 Plan, covering both the 2019 Plan and the 2016 Plan. Options to purchase 1,386,592 shares of common stock, at exercise prices ranging from $10.00 to $22.20 per share, or a weighted-average exercise price of $12.75 per share, were outstanding under the 2019 Plan. Options to purchase 2,693,296 shares of common stock, at exercise prices ranging from $0.04 to $12.93 per share, or a weighted-average exercise price of $3.76 per share, were outstanding under the 2016 Plan.

Shares subject to stock awards granted under our 2019 Plan that expire or terminate without being exercised in full or that are paid out in cash rather than in shares do not reduce the number of shares available for issuance under our 2019 Plan. If any shares of common stock issued pursuant to a stock award are forfeited back to or repurchased or

reacquired by us for any reason, the shares that are forfeited or repurchased or reacquired will revert to and again become available for issuance under the 2019 Plan. Any shares reacquired in satisfaction of tax withholding obligations or as consideration for the exercise or purchase price of a stock award will again become available for issuance under the 2019 Plan.

The maximum number of shares of common stock subject to stock awards granted under the 2019 Plan or otherwise during any one calendar year to any non-employee director, taken together with any cash fees paid by us to such non-employee director during such calendar year for service on the board of directors, will not exceed $750,000 in total value (calculating the value of any such stock awards based on the grant date fair value of such stock awards for financial reporting purposes), or, with respect to the calendar year in which a non-employee director is first appointed or elected to our board of directors, $1,100,000.

Plan Administration. The compensation committee of our board of directors has generally administered the 2019 Plan and is referred to as the "plan administrator" herein. The compensation committee of our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than officers) to receive specified stock awards and (2) determine the number of shares subject to such stock awards. Under our 2019 Plan, our board of directors has the authority to determine award recipients, grant dates, the numbers and types of stock awards to be granted, the applicable fair market value, and the provisions of each stock award, including the period of exercisability and the vesting schedule applicable to a stock award.

Under the 2019 Plan, the board of directors also generally has the authority to effect, with the consent of any adversely affected participant, (1) the reduction of the exercise, purchase, or strike price of any outstanding award; (2) the cancellation of any outstanding award and the grant in substitution therefore of other awards, cash, or other consideration; or (3) any other action that is treated as a repricing under U.S. GAAP.

Stock Options. ISOs and NSOs are granted under stock option agreements adopted by the plan administrator. The plan administrator determines the exercise price for stock options, within the terms and conditions of the 2019 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2019 Plan vest at the rate specified in the stock option agreement as determined by the plan administrator.

The plan administrator determines the term of stock options granted under the 2019 Plan, up to a maximum of 10 years. Unless the terms of an optionholder's stock option agreement provide otherwise, if an optionholder's service relationship with us or any of our affiliates ceases for any reason other than disability, death, or cause, the optionholder may generally exercise any vested options for a period of three months following the cessation of service. This period may be extended in the event that exercise of the option is prohibited by applicable securities laws or our insider trading policy. If an optionholder's service relationship with us or any of our affiliates ceases due to death, or an optionholder dies within a certain period following cessation of service, the optionholder or a beneficiary may generally exercise any vested options for a period of 18 months following the date of death. If an optionholder's service relationship with us or any of our affiliates ceases due to disability, the optionholder may generally exercise any vested options for a period of 12 months following the cessation of service. In the event of a termination for cause, options generally terminate upon the termination date. In no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of common stock issued upon the exercise of a stock option will be determined by the plan administrator and may include (1) cash, check, bank draft or money order, (2) a broker-assisted cashless exercise, (3) the tender of shares of our common stock previously owned by the optionholder, (4) a net exercise of the option if it is an NSO or (5) other legal consideration approved by the plan administrator.

Unless the plan administrator provides otherwise, options generally are not transferable except by will or the laws of descent and distribution. Subject to approval of the plan administrator or a duly authorized officer in each case, (i) an option may be transferred pursuant to a domestic relations order, official marital settlement agreement, or other divorce or separation instrument and (ii) an optionholder may designate a beneficiary who may exercise the option following the optionholder's death.

Tax Limitations on ISOs. The aggregate fair market value, determined at the time of grant, of our common stock with respect to ISOs that are exercisable for the first time by an award holder during any calendar year under all of our stock plans may not exceed $100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the stock subject to the option on the date of grant, and (2) the term of the ISO does not exceed five years from the date of grant.

Restricted Stock Unit Awards. Restricted stock unit awards are granted under restricted stock unit award agreements adopted by the plan administrator. Restricted stock unit awards may be granted in consideration for any form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. A restricted stock unit award may be settled by cash, delivery of stock, a combination of cash and stock as deemed appropriate by the plan administrator, or in any other form of consideration set forth in the restricted stock unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted stock unit award. Except as otherwise provided in the applicable award agreement, restricted stock unit awards that have not vested will be forfeited once the participant's continuous service ends for any reason.

Restricted Stock Awards. Restricted stock awards are granted under restricted stock award agreements adopted by the plan administrator. A restricted stock award may be awarded in consideration for cash, check, bank draft or money order, past or future services to us, or any other form of legal consideration that may be acceptable to our board of directors and permissible under applicable law. The plan administrator determines the terms and conditions of restricted stock awards, including vesting and forfeiture terms. If a participant's service relationship with us ends for any reason, we may receive any or all of the shares of common stock held by the participant that have not vested as of the date the participant terminates service with us through a forfeiture condition or a repurchase right.

Stock Appreciation Rights. Stock appreciation rights are granted under stock appreciation right agreements adopted by the plan administrator. The plan administrator determines the purchase price or strike price for a stock appreciation right, which generally cannot be less than 100% of the fair market value of our common stock on the date of grant. A stock appreciation right granted under the 2019 Plan vests at the rate specified in the stock appreciation right agreement as determined by the plan administrator.

The plan administrator determines the term of stock appreciation rights granted under the 2019 Plan, up to a maximum of 10 years. If a participant's service relationship with us or any of our affiliates ceases for any reason other than cause, disability, or death, the participant may generally exercise any vested stock appreciation right for a period of three months following the cessation of service. This period may be further extended in the event that exercise of the stock appreciation right following such termination of service is prohibited by applicable securities laws or our insider trading policy. If a participant's service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested stock appreciation right for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, stock appreciation rights generally terminate immediately upon the occurrence of the event giving rise to the termination of the individual for cause. In no event may a stock appreciation right be exercised beyond the expiration of its term.

Performance Awards. The 2019 Plan permits the grant of performance-based stock and cash awards. Our compensation committee may structure awards so that the stock or cash will be issued or paid only following the achievement of certain pre-established performance goals during a designated performance period.

The performance goals that may be selected include one or more of the following: (i) sales; (ii) revenues; (iii) assets; (iv) expenses; (v) market penetration or expansion; (vi) earnings from operations; (vii) earnings before or after deduction for all or any portion of interest, taxes, depreciation, amortization, incentives, service fees or extraordinary or special items, whether or not on a continuing operations or an aggregate or per share basis; (viii) net income or net income per common share (basic or diluted); (ix) return on equity, investment, capital or assets; (x) one or more operating ratios; (xi) borrowing levels, leverage ratios or credit rating; (xii) market share; (xiii) capital expenditures; (xiv) cash flow, free cash flow, cash flow return on investment, or net cash provided by operations;

(xv) stock price, dividends or total stockholder return; (xvi) development of new technologies or products; (xvii) sales of particular products or services; (xviii) economic value created or added; (xix) operating margin or profit margin; (xx) customer acquisition or retention; (xxi) raising or refinancing of capital; (xxii) successful hiring of key individuals; (xxiii) resolution of significant litigation; (xxiv) acquisitions and divestitures (in whole or in part); (xxv) joint ventures and strategic alliances; (xxvi) spin-offs, split-ups and the like; (xxvii) reorganizations; (xxviii) recapitalizations, restructurings, financings (issuance of debt or equity) or refinancings; (xxix) strategic business criteria, consisting of one or more objectives based on the following goals: achievement of timely development, design management or enrollment, meeting specified market penetration or value added, payor acceptance, patient adherence, peer reviewed publications, issuance of new patents, establishment of or securing of licenses to intellectual property, product development or introduction (including, without limitation, any clinical trial accomplishments, regulatory or other filings, approvals or milestones, discovery of novel products, maintenance of multiple products in pipeline, product launch or other product development milestones), geographic business expansion, cost targets, cost reductions or savings, customer satisfaction, operating efficiency, acquisition or retention, employee satisfaction, information technology, corporate development (including, without limitation, licenses, innovation, research or establishment of third party collaborations), manufacturing or process development, legal compliance or risk reduction, patent application or issuance goals, or goals relating to acquisitions, divestitures or other business combinations (in whole or in part), joint ventures or strategic alliances; and (xxx) other measures of performance selected by the board of directors.

The performance goals may be based on company-wide performance or performance of one or more business units, divisions, affiliates, or business segments, and may be either absolute or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Our board of directors is authorized at any time in its sole discretion, to adjust or modify the calculation of a performance goal for such performance period in order to prevent the dilution or enlargement of the rights of participants, (a) in the event of, or in anticipation of, any unusual or extraordinary corporate item, transaction, event or development; (b) in recognition of, or in anticipation of, any other unusual or nonrecurring events affecting us, or our financial statements in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles, or business conditions; or (c) in view of the board of director's assessment of our business strategy, performance of comparable organizations, economic and business conditions, and any other circumstances deemed relevant. Specifically, the board of directors is authorized to make adjustments in the method of calculating attainment of performance goals and objectives for a performance period as follows: (i) to exclude the dilutive effects of acquisitions or joint ventures; (ii) to assume that any business divested by us achieved performance objectives at targeted levels during the balance of a performance period following such divestiture; and (iii) to exclude the effect of any change in the outstanding shares of our common stock by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends. In addition, the board of directors is authorized to make adjustments in the method of calculating attainment of performance goals and objectives for a performance period as follows: (i) to exclude restructuring and/or other nonrecurring charges; (ii) to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated net sales and operating earnings; to exclude the effects of changes to generally accepted accounting standards required by the Financial Accounting Standards Board; (iv) to exclude the effects of any items that are "unusual" in nature or occur "infrequently" as determined under U.S. GAAP; (v) to exclude the effects to any statutory adjustments to corporate tax rates; and (vi) to make other appropriate adjustments selected by the board of directors.

Other Stock Awards. The plan administrator may grant other awards based in whole or in part by reference to our common stock. The plan administrator will set the number of shares under the stock award and all other terms and conditions of such awards.

Changes to Capital Structure. In the event there is a specified type of change in our capital structure, such as a stock split, reverse stock split, or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2019 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued on the exercise of ISOs and (4) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding stock awards.

Corporate Transactions. Our 2019 Plan provides that in the event of certain specified significant corporate transactions (or a change in control, as defined below), unless otherwise provided in an award agreement or other written agreement between us and the award holder, the plan administrator may take one or more of the following actions with respect to such stock awards:

- arrange for the assumption, continuation, or substitution of a stock award by a successor corporation;
- arrange for the assignment of any reacquisition or repurchase rights held by us to a successor corporation;
- accelerate the vesting, in whole or in part, of the stock award and provide for its termination if not exercised (if applicable) at or before the effective time of the transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us;
- cancel or arrange for the cancellation of the stock award, to the extent not vested or not exercised before the effective time of the transaction, in exchange for a cash payment, if any; or
- make a payment equal to the excess, if any, of (A) the value of the property the participant would have received on exercise of the award immediately before the effective time of the transaction, over (B) any exercise price payable by the participant in connection with the exercise.

The plan administrator is not obligated to treat all stock awards or portions of stock awards in the same manner and is not obligated to take the same actions with respect to all participants.

Under the 2019 Plan, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger or consolidation where we do not survive the transaction, or (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

Change in Control. In the event of a change in control, the plan administrator may take any of the above-mentioned actions. Awards granted under the 2019 Plan may be subject to additional acceleration of vesting and exercisability upon or after a change in control as may be provided in the applicable stock award agreement or in any other written agreement between us or any affiliate and the participant, but in the absence of such provision, no such acceleration will automatically occur. Under the 2019 Plan, a change in control is generally (1) the acquisition by any person or company of more than 50% of the combined voting power of our then outstanding stock, (2) a merger, consolidation or similar transaction in which our stockholders immediately before the transaction do not own, directly or indirectly, more than 50% of the combined voting power of the surviving entity (or the parent of the surviving entity) in substantially the same proportions as their ownership immediately prior to such transaction, (3) a sale, lease, exclusive license or other disposition of all or substantially all of our assets other than to an entity more than 50% of the combined voting power of which is owned by our stockholders in substantially the same proportions as their ownership of our outstanding voting securities immediately prior to such transaction, (4) a complete dissolution or liquidation of the company or (5) when a majority of our board of directors becomes comprised of individuals who were not serving on our board of directors on the date of the underwriting agreement related to the IPO, or the incumbent board, or whose nomination, appointment, or election was not approved by a majority of the incumbent board still in office.

Plan Amendment or Termination. Our board of directors has the authority to amend, suspend, or terminate our 2019 Plan; provided that such action does not materially impair the existing rights of any participant without such participant's written consent. Certain material amendments also require the approval of our stockholders. No ISOs may be granted after the tenth anniversary of the date our board of directors adopts our 2019 Plan. No stock awards may be granted under our 2019 Plan while it is suspended or after it is terminated.

2016 Equity Incentive Plan

General. Our board of directors adopted and our stockholders initially approved the 2016 Plan in June 2016. Our board of directors subsequently amended the 2016 Plan in December 2016, June 2018 and November 2018 (and our stockholders subsequently approved the amendments to the 2016 Plan in December 2016 and April 2019) the purpose of which was to increase the number of shares available for issuance under the 2016 Plan (the June 2018 amendment also amended the 2016 Plan to accelerate in full, all options granted under the plan, upon a change of control (as defined in the 2016 Plan)). The 2016 Plan was terminated in connection with our adoption of the 2019 Plan; however, awards outstanding under the 2016 Plan continue in full effect in accordance with their existing terms. As a result, no additional awards under the 2016 Plan will be granted and all outstanding stock awards granted under the 2016 Plan that are repurchased, forfeited, expired or are cancelled will become available for grant under the 2019 Plan in accordance with its terms. The 2016 Plan will continue to govern outstanding equity awards granted thereunder.

Administration. Our board of directors has administered the 2016 Plan since its adoption, however, following the IPO, the compensation committee of our board of directors has generally administered the 2016 Plan. Our compensation committee has full authority and discretion to take any actions it deems necessary or advisable for the administration of the 2016 Plan. Our compensation committee may modify, extend or renew outstanding options or may accept the cancellation of outstanding options (whether granted by us or another issuer) in return for the grant of new options for the same or a different number of shares and at the same or a different exercise price.

Types of Awards. The 2016 Plan provides for the grant of incentive stock options and nonstatutory stock options to purchase shares of our common stock, equity appreciation rights awards, restricted stock awards, restricted stock units, performance awards and other stock-based awards to employees, members of our board of directors and consultants. Incentive stock options may be granted only to employees.

Options. The exercise price of options granted under the 2016 Plan may not be less than 100% of the fair market value of our common stock on the grant date. Options expire at the time determined by the administrator, but in no event more than ten years after they are granted, and generally expire earlier if the optionholder’s service terminates.

Changes in Capitalization. If we at any time change the number of shares of common stock issued without new consideration (such as by stock dividend or stock split), the total number of shares of common stock reserved for issuance under the 2016 Plan, the maximum number of shares of common stock which may be made subject to incentive stock options during the term of the 2016 Plan, and the number of shares of common stock covered by each then outstanding award will be equitably adjusted and the aggregate consideration payable to us, if any, will not be changed.

Corporate Transactions. Unless in connection with a change of control, in the event of any merger, consolidation or reorganization of us with or into another entity other than a merger, consolidation or reorganization in which we are the continuing entity and which does not result in the outstanding shares of our common stock being converted into or exchanged for different securities, cash or other property, or any combination thereof, we may substitute, on an equitable basis for each share of common stock then subject to an outstanding award, the number and the kind of shares of stock, other securities, cash or other property to which holders of shares of common stock will be entitled pursuant to the transaction.

Change of Control. Unless otherwise expressly provided in the applicable award agreement governing an award, upon a change of control, our board of directors (or a committee thereof) may:

- provide for the acceleration of vesting with respect to, all or any portion of an award;
- cancel an award for a cash payment equal to the fair market value which, in the case of stock options will be deemed to be equal to the excess, if any, of the value of the consideration to be paid in the change of control transaction to holders of the same number of shares of common stock subject to the options over the aggregate exercise price;

- provide for the issuance of a substitute award that will substantially preserve the otherwise applicable terms of any affected award;
- terminate unvested stock options without providing accelerated vesting; or
- take any other action with respect to the awards our board of directors or committee deems appropriate.

The treatment of awards upon a change of control may vary among the award types and participants in the sole discretion of our board of directors.

In general, a "change of control" means the acquisition of the company by another entity by means of any transaction or series of related transactions, unless our stockholders of record immediately prior to such transaction or series of related transactions hold, immediately after such transaction or series of related transactions, at least 50% of the voting power of the surviving or acquiring entity; or a sale of all or substantially all of our assets, subject to certain exceptions.

Transferability. A participant may not transfer stock awards under the 2016 Plan other than by will, the laws of descent and distribution, or as otherwise provided under the 2016 Plan.

Plan Amendment or Termination. Our board of directors has the authority to amend, suspend or terminate the 2016 Plan, provided that such action is approved by our stockholders to the extent stockholder approval is necessary. As described above, the 2016 Plan will terminate upon the effective date of the 2019 Plan.

2019 Employee Stock Purchase Plan

Our board of directors adopted, the 2019 Employee Stock Purchase Plan, or the ESPP, on April 24, 2019 and our stockholders subsequently approved the ESPP on April 26, 2019. The ESPP became effective immediately prior to the date of the underwriting agreement related to the IPO. The purpose of the ESPP is to secure the services of new employees, to retain the services of existing employees, and to provide incentives for such individuals to exert maximum efforts toward our success and that of our affiliates. The ESPP qualifies as an "employee stock purchase plan" within the meaning of Section 423 of the Code for U.S. employees.

Share Reserve. Following the IPO, the ESPP authorized the issuance of 180,000 shares of our common stock under purchase rights granted to our employees or to employees of any of our designated affiliates. The number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2020 through January 1, 2029, by the lesser of (1) 1% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of the automatic increase and (2) 360,000 shares; provided that before the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (1) and (2). As of the date hereof, no shares of our common stock have been purchased under the ESPP.

Administration. Our board of directors administers the ESPP and may delegate its authority to administer the ESPP to our compensation committee. The ESPP is implemented through a series of offerings under which eligible employees are granted purchase rights to purchase shares of our common stock on specified dates during such offerings. Under the ESPP, we may specify offerings with durations of not more than 27 months, and may specify shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for employees participating in the offering. An offering under the ESPP may be terminated under certain circumstances.

Payroll Deductions. Generally, all regular employees, including executive officers, employed by us or by any of our designated affiliates, may participate in the ESPP and may contribute, normally through payroll deductions, up to 15% of their earnings (as defined in the ESPP) for the purchase of our common stock under the ESPP. Unless otherwise determined by our board of directors, common stock will be purchased for the accounts of employees participating in the

ESPP at a price per share that is at least the lesser of (1) 85% of the fair market value of a share of our common stock on the first date of an offering or (2) 85% of the fair market value of a share of our common stock on the date of purchase.

Limitations. Employees may have to satisfy one or more of the following service requirements before participating in the ESPP, as determined by our board of directors, including: (1) being customarily employed for more than 20 hours per week, (2) being customarily employed for more than five months per calendar year or (3) continuous employment with us or one of our affiliates for a period of time (not to exceed two years). No employee may purchase shares under the ESPP at a rate in excess of $25,000 worth of our common stock based on the fair market value per share of our common stock at the beginning of an offering for each calendar year such a purchase right is outstanding. Finally, no employee will be eligible for the grant of any purchase rights under the ESPP if immediately after such rights are granted, such employee has voting power over 5% or more of our outstanding capital stock measured by vote or value under Section 424(d) of the Code.

Changes to Capital Structure. In the event that there occurs a change in our capital structure through such actions as a stock split, merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, liquidating dividend, combination of shares, exchange of shares, change in corporate structure, or similar transaction, the board of directors will make appropriate adjustments to: (1) the class(es) and maximum number of shares reserved under the ESPP, (2) the class(es) and maximum number of shares by which the share reserve may increase automatically each year, (3) the class(es) and number of shares subject to and purchase price applicable to outstanding offerings and purchase rights and (4) the class(es) and number of shares that are subject to purchase limits under ongoing offerings.

Corporate Transactions. In the event of certain significant corporate transactions, any then-outstanding rights to purchase our stock under the ESPP may be assumed, continued, or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue, or substitute for such purchase rights, then the participants' accumulated payroll contributions will be used to purchase shares of our common stock within 10 business days before such corporate transaction, and such purchase rights will terminate immediately.

Under the ESPP, a corporate transaction is generally the consummation of: (1) a sale of all or substantially all of our assets, (2) the sale or disposition of more than 50% of our outstanding securities, (3) a merger or consolidation where we do not survive the transaction and (4) a merger or consolidation where we do survive the transaction but the shares of our common stock outstanding immediately before such transaction are converted or exchanged into other property by virtue of the transaction.

ESPP Amendment or Termination. Our board of directors has the authority to amend or terminate our ESPP, provided that except in certain circumstances such amendment or termination may not materially impair any outstanding purchase rights without the holder's consent. We will obtain stockholder approval of any amendment to our ESPP as required by applicable law or listing requirements.

Non-Employee Director Compensation

Prior to April 2019, we did not have a formal compensation policy with respect to service on our board of directors, but we reimbursed our non-employee directors for direct expenses incurred in connection with attending meetings of our board of directors or its committees, and occasionally granted stock options.

In April 2019, our board of directors approved a non-employee director compensation policy that became effective in connection with the IPO. Under this policy, we pay each of our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairperson of each committee receives a higher retainer for such service. These retainers are payable in arrears in four equal quarterly installments on the last day of each quarter; provided that the amount of such payment is prorated for any portion of such quarter that the director is not serving on our board of directors or the applicable committee. No retainers were paid in respect of any period prior to the completion of the IPO. The retainers to be paid to non-employee directors

for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

Position	Annual Service Retainer	Chairperson Additional Retainer
Board of Directors	$ 40,000	$ —
Audit committee	7,500	15,000
Compensation committee	6,000	12,000
Nominating and corporate governance committee	4,000	8,000

In addition, under our non-employee director compensation policy, each non-employee director elected to our board of directors after the completion of the IPO received an option to purchase 20,460 shares of our common stock. In connection with the IPO, each of our non-employee directors also received options to purchase 20,460 shares of our common stock under our 2019 Plan upon the pricing of the IPO with an exercise price per share equal to the initial public offering price per share. The shares subject to each such stock option will vest monthly over a three-year period, subject to the director's continued service as a director. Further, on the date of each annual meeting of stockholders held after the completion of the IPO, each non-employee director that continues to serve as a non-employee director will receive an option to purchase 10,230 shares of our common stock. The shares subject to each such stock option will vest in equal monthly installments over the 12 months following the date of grant and, notwithstanding the foregoing, will be fully vested on the date of Company's next annual stockholder meeting, subject to the director's continued service as a director. The exercise price per share of these options will equal the fair market value of our common stock on the date of grant. All options granted under this policy will vest in full upon the occurrence of a change in control (as defined in the 2019 Plan) prior to the termination of the director's continuous service.

This policy is intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

2019 Director Compensation Table

The following table sets forth information regarding the compensation earned for service on our board of directors by our non-employee directors during the year ended December 31, 2019. Dr. Shendelman also served on our board of directors, but did not receive any additional compensation for their service as a director and therefore is not included in the table below. The compensation for Dr. Shendelman as a named executive officer is set forth above under "—Summary Compensation Table."

Name	Director Compensation ($)	Option Awards[2] ($)	Total ($)
Les Funtleyder	23,333	601,713 (3)	625,046
Franklin M. Berger, CFA (1)	—	114,197 (4)	114,197
Joel S. Marcus	33,942	240,026 (5)	273,968
Teena Lerner, Ph.D.	38,555	240,026 (5)	278,581
Stacy J. Kanter	38,440	125,829 (6)	164,269
Jay Skyler	34,796	125,829 (6)	160,625

(1) Mr. Berger was a member of our board of directors until the date of the IPO.

(2) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during fiscal year 2019 computed in accordance with ASC 718. Assumptions used in the calculation of these amounts are included in the notes to our financial statements included elsewhere in this Annual Report. These amounts do not reflect the actual economic value that will be realized by our non-employee directors upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.

(3) Represents an option to purchase 27,624 shares of our common stock granted in March 2018 at an exercise price of $1.44 per share.

(4) Represents an option to purchase 35,911 shares of our common stock granted in March 2019 at an exercise price of $4.70 per share.

(5) Represents options to purchase 35,911 shares of our common stock granted in March 2019 at an exercise price of $4.70 per share and 20,460 shares of our common stock granted in May 2019 at an exercise price of $10.00 per share.

(6) Represents an option to purchase 20,460 shares of our common stock granted in May 2019 at an exercise price of $10.00 per share.

The following table provides information regarding the number of shares of common stock underlying stock options granted to our non-employee directors that were outstanding as of December 31, 2019.

Name	Option Awards Outstanding at December 31, 2019
Les Funtleyder	198,414 (2)
Franklin M. Berger, CFA (1)	—
Joel S. Marcus	78,824 (3)
Teena Lerner, Ph.D.	78,824 (3)
Stacy J. Kanter	20,460 (4)
Jay Skyler	20,460 (4)

(1) Mr. Berger was a member of our board of directors until the date of the IPO.

(2) Represents (i) an option to purchase 18,453 shares of our common stock granted June 22, 2016, which was fully vested as of December 31, 2019; (ii) an option to purchase 159,502 shares of our common stock granted March 7, 2019, of which three-fourths were vested as of December 31, 2019 and the remainder vests on March 7, 2020; and (iii) an option to purchase 20,460 shares of our common stock granted on June 4, 2019, of which six-thirty-sixths were vested as of December 31, 2019 and the remainder vests monthly thereafter in one-thirty-sixth increments.

(3) Represents (i) an option to purchase 18,453 shares of our common stock granted March 21, 2017, which was fully vested as of December 31, 2019; (ii) an option to purchase 35,911 shares of our common stock granted March 18, 2019, of which one-third was fully vested as of December 31, 2019 and the remainder vests yearly in one-third increments; and (iii) an option to purchase 20,460 shares of our common stock granted May 13, 2019, of which seven-thirty-sixths were vested as of December 31, 2019 and the remainder vests monthly thereafter in one thirty-sixth increments.

(4) Represents an option to purchase 20,460 shares of our common stock granted May 13, 2019, of which seven-thirty-sixths were vested as of December 31, 2019 and the remainder vests monthly thereafter in one-thirty-sixth increments.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell our common shares on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from them. The director or officer may amend a Rule 10b5-1 plan in some circumstances and may terminate a plan at any time. Our directors and executive officers also may buy or sell additional shares outside of a Rule 10b5-1 plan when

they are not in possession of material nonpublic information subject to compliance with the terms of our insider trading policy.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

The following table sets forth information regarding beneficial ownership of our common stock as of February 29, 2020 by:

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

The percentage ownership information is based on 21,969,277 shares of common stock outstanding as of February 29, 2020. Other information required by this item will be set forth in our definitive Proxy Statement to be filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference to our Proxy Statement.

Information with respect to beneficial ownership has been furnished by each director, officer or beneficial owner of more than 5% of our common stock. We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of our common stock issuable pursuant to the exercise of stock options or warrants that are either immediately exercisable or exercisable within 60 days of February 29, 2020. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them. Except as otherwise noted below, the address for each person or entity listed in the table is c/o Applied Therapeutics, Inc., 545 5th Avenue, Suite 1400, New York, New York 10017.

Greater than 5% Stockholders:	**Number of Shares Beneficially Owned**	**Percentage of Shares Beneficially Owned**
Shoshana Shendelman, Ph. D. (1)	6,295,274	19.7%
Entities affiliated with Alexandria Venture (2)	3,390,576	14.1%
Directors and Named Executive Officers:		
Stacy J. Kanter (3)	12,752	*
Les Funtleyder (4)	209,957	*
Teena Lerner, Ph. D. (5)	76,986	*
Joel S. Marcus (2) (6)	463,176	1.9%
Riccardo Perfetti, M.D., Ph.D. (7)	282,635	1.2%
Jay S. Skyler, M.D., MACP (8)	6,252	*
Mark J. Vignola, Ph.D. (9)	53,865	*
Adam Hansard	—	—
All current executive officers and directors as a group (nine persons) (10)	7,400,897	30.8%

* Represents beneficial ownership of less than 1%.

(1) Includes (a) 3,304,285 shares of common stock held by Dr. Shendelman, (b) 88,397 shares held by Clearpoint Strategy Group LLC, of which Dr. Shendelman is the sole owner, (c) 1,492,094 shares of common stock held by Sycamore Family I LLC, of which Dr. Shendelman's spouse, Vladimir Shendelman, is the sole manager and (d) 1,410,498 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020. Dr. Shendelman may be deemed to have voting and investment power with respect to the shares owned by Sycamore Family I LLC, but disclaims beneficial ownership of such shares.

(2) Includes (a) 1,171,599 shares held by Alexandria Venture Investments, LLC (" Alexandria Venture"), and (b) 2,218,977 shares held by Alexandria Equities No. 7, LLC (" Alexandria Equities," and together with Alexandria Venture, the " Alexandria Entities"). One of our directors, Joel S. Marcus, is the Executive Chairman and founder of Alexandria Real Estate Equities, Inc., the managing member of Alexandria Venture and the parent company of ARE-QRS Corp., which is the general partner of Alexandria Real Estate Equities L.P., which is the managing member of ARE-Special Services, LLC, which is the managing member of Alexandria Equities. ARE-QRS Corp. has full voting and investment power with respect to the shares owned by the Alexandria Equities and Alexandria Real Estate Equities, Inc. has full voting and investment power with respect to the shares owned by the Alexandria Venture. As Executive Chairman and founder of Alexandria Real Estate Equities, Inc., Mr. Marcus may be deemed to have voting and investment power with respect to the shares owned by the Alexandria Entities. Mr. Marcus disclaims beneficial ownership of the shares held by Alexandria Entities, except to the extent of his underlying pecuniary interest therein. The address for the Alexandria Entities is 385 E. Colorado Blvd., Suite 299, Pasadena, California 91101.

(3) Includes 6,252 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020.

(4) Includes 192,809 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020.

(5) Includes 27,393 shares of common stock underlying outstanding options that are immediately exercisable or will become exercisable within 60 days of February 29, 2020.

(6) Includes 57,816 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020.

(7) Includes 282,635 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020.

(8) Includes 6,252 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020.

(9) Includes 53,865 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020.

(10) Includes an aggregate of 2,037,519 shares of common stock underlying outstanding options that are immediately exercisable or will be immediately exercisable within 60 days of February 29, 2020, held by nine executive officers and directors.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

The following sets forth information related to certain relationships and related transactions and our board of directors. Other information required by this item will be set forth in our definitive Proxy Statement to be filed within

120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference to our Proxy Statement.

Certain Relationships and Related Transactions

The following includes a summary of transactions since January 20, 2016 (date of inception) and any currently proposed transactions, to which we were or are to be a participant, in which (1) the amount involved exceeded or will exceed the lesser of (i) $120,000 or (ii) 1% of the average of our total assets for the last two completed fiscal years, and (2) any of our directors, executive officers or holders of more than 5% of our capital stock, or any affiliate or member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described under the section titled “Executive and Director Compensation.”

We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that we would pay or receive, as applicable, in arm’s-length transactions.

Columbia University License Agreements

In October 2016, we entered into the 2016 Columbia Agreement, whereby, among other things, Columbia University granted to us an exclusive license under certain patents, and a non-exclusive license to certain know-how, in each case to develop, manufacture, and commercialize ARI products, including AT-001, AT-003 and AT-007. As partial consideration of Columbia University’s execution and delivery of the 2016 Columbia Agreement, Columbia University was issued 486,077 shares of our common stock, the approximate fair value of which was $0.5 million. See the section titled “Business—Exclusive License Agreement with Columbia University” for more information on the 2016 Columbia Agreement.

In January 2019, we entered into a second license agreement with Columbia University, or the 2019 Columbia Agreement, whereby, among other things, Columbia University granted to us an exclusive license under certain patents, and a non-exclusive license to certain know-how, in each case to develop, manufacture and commercialize PI3K inhibitor products. As consideration, we made a nominal upfront payment to Columbia University. See our financial statements included elsewhere in this Annual Report for more information on the 2019 Columbia Agreement.

Preferred Stock and Warrant Financings and Convertible Note and Warrant Financing

Series A Preferred Stock Financing and Warrants

Between January and March 2017, we issued an aggregate of 3,093,898 shares of our Series A Preferred Stock at a price per share of $2.26 in five closings for total gross proceeds of $7.0 million. The first two closings occurred in January 2017, at which time we issued an aggregate of 2,299,266 shares of our Series A Preferred Stock for gross cash proceeds of approximately $5.2 million. The third and fourth closings occurred in February 2017, at which time we issued an additional 749,496 shares of our Series A Preferred Stock for gross cash proceeds of approximately $1.7 million. The fifth closing occurred in March 2017, at which time we issued an additional 45,137 shares of our Series A Preferred Stock for gross cash proceeds of $0.1 million. In connection with the last closing of the Series A Preferred Stock financing and pursuant to that certain Placement Agency Agreement by and between us and Brookline Capital Markets, a division of CIM Securities, LLC, or Brookline, serving as placement agent, dated October 7, 2016, as amended and restated on November 23, 2016, in March 2017, certain employees of Brookline were issued 10-year warrants, entitling such individuals to purchase up to an aggregate of 309,389 shares of our common stock at an exercise price of $2.49 per share.

The table below sets forth the number of shares of our Series A Preferred Stock purchased by our directors, holders of more than 5% of our capital stock and their affiliated entities or immediate family members. Each share of Series A Preferred Stock in the table below automatically converted into one share of our common stock immediately

upon the completion of the IPO. For a description of the material rights and privileges of the Series A Preferred Stock see Note 4 to the notes to our financial statements included elsewhere in this Annual Report.

Name	Series A Preferred Stock (#)	Aggregate Cash Purchase Price ($)
Franklin M. Berger, CFA[1]	244,032	552,125
Joel S. Marcus[2]	110,497	250,000
Alexandria Venture Investments, LLC[2]	800,716	1,811,625

(1) Mr. Berger was a member of our board of directors until the date of the IPO.

(2) Mr. Marcus, a member of our board of directors, is the Executive Chairman and founder of Alexandria Real Estate Equities, Inc., the managing member of Alexandria Venture Investments, LLC, or Alexandria Venture. Alexandria Real Estate Equities, Inc. has full voting and investment power with respect to the shares owned by the Alexandria Venture.

Convertible Note Financing and Warrants

In February 2018, we issued an aggregate principal amount of $6.0 million of convertible notes in two closings, or the 2018 Notes. The first closing occurred on February 8, 2018, at which time we issued an aggregate principal amount of $5.7 million in convertible notes. The second closing occurred on February 14, 2018, at which time we issued a principal amount of $0.3 million in one convertible note. The 2018 Notes accrued interest at a rate of 15% per annum. On November 5, 2018, we closed on a portion of the Series B Preferred Stock financing described below. At that time, all 2018 Notes and the then accrued interest totaling approximately $6.6 million were converted into 1,097,721 shares of Series B Preferred Stock. In connection with the closing of the convertible note financing and pursuant to that certain Placement Agency Agreement by and between us and Brookline, dated January 18, 2018, in November 2018, certain employees of Brookline were issued 10-year warrants, entitling such individuals to purchase up to an aggregate of 76,847 shares of our common stock at an exercise price of $6.59 per share.

Series B Preferred Stock Financing and Warrants

Between November 2018 and February 2019, we issued an aggregate of 3,347,052 new shares of our Series B Preferred Stock at a price per share of $7.49 in five closings for total gross cash proceeds of approximately $25.1 million, or the Series B Financing. In connection with the Series B Financing, in November 2018, the $6.0 million of the 2018 Notes and the related $0.6 million of accrued interest converted into 1,097,721 shares of our Series B Preferred Stock. The first two closings of the Series B Financing occurred in November 2018, at which time we issued an aggregate of 2,748,437 new shares of our Series B Preferred Stock for total gross cash proceeds of approximately $20.6 million. The third and fourth closings occurred in December 2018, at which time we issued an aggregate of 155,690 new shares of our Series B Preferred Stock for total gross cash proceeds of approximately $1.2 million. The fifth closing occurred in February 2019, at which time we issued 442,925 shares of our Series B Preferred Stock for total gross cash proceeds of approximately $3.3 million.

In connection with the last closing of the Series B Financing and pursuant to that certain Placement Agency Agreement by and between us and Brookline, dated August 28, 2018, or the Series B Placement Agency Agreement, in April 2019 certain employees of Brookline were issued 10-year warrants, entitling such individuals to purchase up to an aggregate of 96,128 shares of our common stock at an exercise price of $8.24. We have also agreed to issue additional warrants to purchase shares of our common stock to such individuals pursuant to the Series B Placement Agency Agreement for a period through 12 months from the last closing date, which number shall represent (i) 2% of the aggregate number of shares of Series B Preferred Stock sold to our officers, directors and existing investors as of the date of the Series B Placement Agency Agreement and their respective affiliates; (ii) 4% of the aggregate number of shares of Series B Preferred Stock sold to certain agreed upon investors as listed in the Series B Placement Agency Agreement; and (iii) 6% of the aggregate number of shares of Series B Preferred Stock sold to all other investors; and in each case after accounting for the conversion of all such shares of Series B Preferred Stock into our common stock.

The table below sets forth the number of shares of Series B Preferred Stock purchased by our executive officers, directors, holders of more than 5% of our capital stock and their affiliated entities or immediate family members. Each share of our outstanding preferred stock automatically converted into one share of our common stock immediately upon the completion of the IPO. For a description of the material rights and privileges of the Series B Preferred Stock see Note 4 to the notes to our financial statements included elsewhere in this Annual Report.

Name	Series B Preferred Stock (#)	Cancellation of Indebtedness (Note Conversion) ($)	Cash Purchase Price of Series B Preferred Stock ($)	Aggregate Purchase Price ($)
Franklin M. Berger, CFA[1]	294,695	1,272,568	615,955	1,888,523
Affiliates of E Squared[2]	675,744	46,608	5,001,684	5,048,292
Joel S. Marcus[3]	135,192	288,596	651,530	940,126
Entities affiliated with Alexandria Venture[4]	1,614,860	1,673,052	10,000,059	11,673,111

(1) Mr. Berger was a member of our board of directors until the date of the IPO. 212,430 shares of Series B Preferred Stock held by Mr. Berger were issued as a result of the conversion of his 2018 Note.

(2) Consists of (a) 7,734 shares of our Series B Preferred Stock held by Edward Ilyadzhanov and (b) 668,010 shares of our Series B Preferred Stock held by A1, a Series of E Squared Investment Fund, LLC, or A1. 7,734 shares of Series B Preferred Stock held by Mr. Ilyadzhanov were issued as a result of the conversion of his 2018 Note. Mr. Funtleyder, our interim Chief Financial Officer and a member of our board of directors, is a healthcare portfolio manager at E Squared Capital Management, LLC, or E Squared, which is the general manager of A1. Mr. Ilyadzhanov, the founder, Managing Partner and Chief Investment Officer of E Squared, has full voting and investment power with respect to shares owned by A1.

(3) Mr. Marcus is a member of our board of directors. 48,176 shares of Series B Preferred Stock held by Mr. Marcus were issued as a result of the conversion of his 2018 Note.

(4) Consists of (a) 370,883 shares of our Series B Preferred Stock held by Alexandria Venture and (b) 1,243,977 shares of our Series B Preferred Stock held by Alexandria Equities No. 7, LLC, or Alexandria Equities. 279,281 shares of Series B Preferred Stock held by Alexandria Venture were issued as a result of the conversion of its 2018 Note. Mr. Marcus, a member of our board of directors, is the Executive Chairman and founder of Alexandria Real Estate Equities, Inc., the managing member of Alexandria Venture and the parent company of ARE-QRS Corp., which is the general partner of Alexandria Real Estate Equities L.P., which is the managing member of ARE-Special Services, LLC, which is the managing member of the Alexandria Equities. Alexandria Real Estate Equities, Inc. has full voting and investment power with respect to the shares owned by the Alexandria Venture. ARE-QRS Corp. has full voting and investment power with respect to the shares owned by the Alexandria Equities.

Investors' Rights Agreement

We are party to an amended and restated investors' rights agreement, dated November 5, 2018, with the holders of our preferred stock, including our directors, Franklin M. Berger, Teena Lerner, Joel S. Marcus and Les Funtleyder, and all holders of more than 5% of our capital stock. This agreement provides that these holders are entitled to certain registration rights, including the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we otherwise file. In addition to the registration rights, this agreement provides for certain information rights and rights of first offer in favor of certain holders of our outstanding preferred stock with regard to certain issuances of our capital stock. The information rights and rights of first offer terminated upon the completion of the IPO. The registration rights will terminate upon the earliest of (i) the closing of a deemed liquidation event, (ii) with respect to each stockholder, the date when such stockholder can sell all of its registrable shares without limitation during a three-month period without registration pursuant to Rule 144 of the Securities Act or another similar exemption under the Securities Act and (iii) May, 2022.

Other Transactions

We have entered into certain employment-related agreements with our executive officers that, among other things, provide for compensatory and certain change in control benefits. For a description of these agreements and arrangements, see the section titled “Executive and Director Compensation—Employment Arrangements.” We have also entered into agreements with our non-employee directors that provide for compensatory benefits. For a description of these agreements, see the section titled “Executive and Director Compensation—Non-Employee Director Compensation.”

We have also granted stock options to our executive officers and directors. For a description of these stock options, see the section titled “Executive and Director Compensation.”

Indemnification Agreements

We have entered or intend to enter, and intend to continue to enter, into separate indemnification agreements with some of our directors and executive officers, in addition to the indemnification provided for in our bylaws. These indemnification agreements provide our directors and executive officers with contractual rights to indemnification and, in some cases, expense advancement in any action or proceeding arising out of their services as one of our directors or executive officers or as a director or executive officer of any other company or enterprise to which the person provides services at our request.

Related Party Transaction Policy

We have adopted a written related party transaction policy that sets forth our procedures for the identification, review, consideration and approval or ratification of related party transactions. For purposes of this policy only, a “related person transaction” is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which we and any related person are participants involving an amount that exceeds or will exceed the lesser of (1) $120,000 or (2) 1% of the average of our total assets for the last two completed fiscal years. Transactions involving compensation for services provided to us as an employee, consultant or director are not considered related-person transactions under this policy. A “related person” is any executive officer, director, nominee to become a director or a holder of more than 5% of our capital stock, or any affiliate or member of the immediate family of the foregoing.

Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to our audit committee or, where review by our audit committee would be inappropriate due to a conflict of interest, to another independent body of our board of directors, for review. The presentation must include a description of, among other things, all of the parties, the direct and indirect interests of the related persons, the purpose of the transaction, the material facts, the benefits of the transaction to us and whether any alternative transactions are available, an assessment of whether the terms are comparable to the terms available from unrelated third parties and management’s recommendation. To identify related party transactions in advance, we rely on information supplied by our executive officers, directors and certain significant stockholders. In considering related-person transactions, our audit committee or another independent body of our board of directors takes into account the relevant available facts and circumstances including, but not limited to:

- the risks, costs and benefits to us;
- the impact on a director’s independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated;
- the terms of the transaction;
- the availability of other sources for comparable services or products; and

- the terms available to or from, as the case may be, unrelated third parties under the same or similar circumstances.

All of the transactions described in this section were entered into prior to the adoption of this policy. Although we have not had a written policy for the review and approval of transactions with related persons, our board of directors has historically reviewed and approved any transaction where a director or officer had a financial interest, including the transactions described above. Prior to approving such a transaction, the material facts as to a director's or officer's relationship or interest in the agreement or transaction were disclosed to our board of directors. Our board of directors took this information into account when evaluating the transaction and in determining whether such transaction was fair to us and in the best interest of all our stockholders.

Director Independence

Under The Nasdaq Stock Market LLC, or Nasdaq, Marketplace Rules, or the Nasdaq Listing Rules, independent directors must comprise a majority of our board of directors as a public company within one year of listing.

Our board of directors has undertaken a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that none of our directors except Shoshana Shendelman, representing one of our six directors, will have any relationships that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is " independent" as that term is defined under the applicable rules and regulations of the SEC and the listing requirements of the Nasdaq Listing Rules. Our board of directors has determined that Dr. Shendelman, by virtue of her position as our President and Chief Executive Officer, is not independent under applicable rules and regulations of the SEC and the Nasdaq Listing Rules. In making this determination, our board of directors considered the current and prior relationships that each non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director, and in the case of Mr. Funtleyder, the fact that he was our former Interim Chief Financial Officer.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES.

The information required by this Item will be set forth in our definitive Proxy Statement under the caption "Independent Registered Public Accounting Firm", to be filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, and is incorporated herein by reference to our Proxy Statement.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

(a) The following documents are filed as part of this Annual Report

1. Financial Statements:

The following financial statements and schedules of the Registrant are contained in Part II, Item 8, “Financial Statements and Supplementary Data” of this Annual Report:

Item	Page
Report of Independent Registered Public Accounting Firm	F-1
Consolidated Balance Sheets as of December 31, 2019 and 2018	F-2
Consolidated Statements of Operations for the years ended December 31, 2019, 2019 and 2018	F-3
Consolidated Statements of Comprehensive Income for the years ended December 31, 2019, 2019 and 2018	F-4
Consolidated Statements of Cash Flows for the years ended December 31, 2019, 2019 and 2018	F-6
Consolidated Statement of Changes in Shareholders’ Equity for the years ended December 31, 2019, and 2018	F-5
Notes to Consolidated Financial Statements	F-7

2. Financial Statement Schedules:

There are no Financial Statement Schedules included with this filing for the reason that they are not applicable or are not required or the information is included in the financial statements or notes thereto.

(b) Exhibits required by Item 601 of Regulation S-K

The information required by this Item is set forth on the exhibit index that follows the signature page of this Annual Report.

EXHIBIT INDEX

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date
3.1+	Amended and Restated Certificate of Incorporation of the Registrant, as amended.	8-K	001-38898	3.1	May 16, 2019
3.2+	Amended and Restated Bylaws of Registrant.	8-K	001-38898	3.2	May 16, 2019
4.1+	Registration Rights Agreement, dated November 7, 2019, by and among the Company and the Purchasers.	8-K	001-38898	10.2	November 12, 2019
4.2+	Form of Common Stock Certificate of Registrant.	10-Q	001-38898	4.2	August 12, 2019
4.3+	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated November 5, 2018.	S-1/A	333-230838	4.2	April 29, 2019
4.4+	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC on March 13, 2017.	S-1/A	333-230838	4.3	April 29, 2019
4.5+	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC on November 5, 2018.	S-1/A	333-230838	4.4	April 29, 2019
4.6+	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC on April 9, 2019.	S-1/A	333-230838	4.5	April 29, 2019
4.7	Description of securities registered under Section 12 of the Exchange Act.				
10.1*+	Forms of Indemnity Agreement by and between the Company and its directors and executive officers.	S-1/A	333-230838	10.1	April 29, 2019
10.2*+	2019 Equity Incentive Plan.	S-1/A	333-230838	10.2	April 29, 2019
10.3*+	Forms of Option Grant Notice and Option Agreement under 2019 Equity Incentive Plan.	S-1/A	333-230838	10.3	April 29, 2019
10.4*+	Form of Restricted Stock Unit Grant Notice and Unit Award Agreement under 2019 Equity Incentive Plan.	S-1/A	333-230838	10.4	April 29, 2019
10.5*+	2016 Equity Incentive Plan, as amended.	S-1/A	333-230838	10.5	April 29, 2019
10.6*+	Forms of Stock Option Agreement under the 2016 Equity Incentive Plan, as amended.	S-1/A	333-230838	10.6	April 29, 2019
10.7*+	2019 Employee Stock Purchase Plan	S-1/A	333-230838	10.7	April 29, 2019

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date
10.8†+	Exclusive License Agreement by and between the Registrant and The Trustees of Columbia University in the City of New York, dated October 26, 2016.	S-1	333-230838	10.11	April 12, 2019
10.9*+	Employment Agreement, by and between the Company Riccardo Perfetti, dated August 28, 2019.	10-Q	001-38898	10.1	November 13, 2019
10.10*+	Employment Agreement by and between the Company and Mark Vignola, dated August 29, 2019.	10-Q	001-38898	10.2	November 13, 2019
10.11*+	Separation Agreement, by and between the Company and Les Funtleyder, dated May 28, 2019.	10-Q	001-38898	10.7	August 12, 2019
10.12+	Securities Purchase Agreement, dated November 7, 2019, by and among the Company and Purchasers.	8-K	001-38898	10.1	November 12, 2019
10.13*	Employment Agreement, by and between the Registrant and Shoshana Shendelman, dated March 9, 2020.				
10.14*	Amendment to Employment Agreement, by and between the Registrant and Riccardo Perfetti, dated March 9, 2020.				
23.1	Consent of Ernst & Young LLP, an Independent Registered Public Accounting Firm.				
31.1	Rule 13a-14(a)/15d-14(a) Certification under the Exchange Act by Shoshana Shendelman, President and Chief Executive Officer (Principal Executive Officer).				
31.2	Rule 13a-14(a)/15d-14(a) Certification under the Exchange Act by Mark J. Vignola, Chief Financial Officer (Principal Financial Officer).				
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 Section 1350 Certifications.				
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 Section 1350 Certifications.				
101.INS	XBRL Instance Document.				
101.SCH	XBRL Taxonomy Extension Schema Document.				

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF	XBRL Taxonomy Extensions Definition Linkbase Document.				
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.				
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.				

* Indicates a management contract or compensatory plan.
† Portions of this exhibit have been omitted.
+ Previously filed.

SIGNATURES

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

Applied Therapeutics, Inc.

Dated: March 13, 2020

/s/ *Shoshana Shendelman*
Name: Shoshana Shendelman, Ph.D.
Title: President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Company and in the capacities indicated on the 13th of March 2020.

Name	Title	Date
/s/ Shoshana Shendelman Shoshana Shendelman, Ph.D.	President and Chief Executive Officer (Principal Executive Officer)	March 13, 2020
/s/ Mark J. Vignola Mark J. Vignola, Ph. D.	Chief Financial Officer (Principal Financial and Accounting Officer)	March 13, 2020
/s/ Les Funtleyder Les Funtleyder	Director	March 13, 2020
/s/ Teena Lerner Teena Lerner, Ph.D.	Director	March 13, 2020
/s/ Stacy Kanter Stacy Kanter	Director	March 13, 2020
/s/ Joel S. Marcus Joel S. Marcus	Director	March 13, 2020
/s/ Jay S. Skyler Jay S. Skyler, M.D., MACP	Director	March 13, 2020

Exhibit 4.7

DESCRIPTION OF APPLIED THERAPEUTICS, INC. SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT

Description of Common Stock

The following is a summary of the rights and preferences of our common stock, and the related provisions of our amended and restated certificate of incorporation and amended and restated bylaws, as each is in effect as the date hereof, copies of which are incorporated by reference as Exhibits 3.1 and 3.2 to our Annual Report on Form 10-K for the year ended December 31, 2019 of which this Exhibit 4.7 is a part. While we believe that the following description covers the material terms of our common stock, the description may not contain all of the information that is important to you. We encourage you to read carefully our amended and restated certificate of incorporation, amended and restated bylaws and the other documents we refer to for a more complete understanding of our common stock.

Except as otherwise indicated or the context otherwise requires, the terms "Company," "us," "we" and "our" refer to Applied Therapeutics, Inc. The rights of our stockholders are generally covered by Delaware law and our amended and restated certificate of incorporation and amended and restated bylaws (each as amended and restated and in effect on the date hereof). The terms of our common stock are therefore subject to Delaware law.

General

Our amended and restated certificate of incorporation provides that we may issue up to 100,000,000 shares of common stock, par value $0.0001 per share. As of December 31, 2019, we had 18,531,560 shares of common stock outstanding.

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of at least 66$^{2}/_{3}$% of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, is required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction. There are no cumulative voting rights.

Dividends

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose on a non-cumulative basis.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Registration Rights

Certain holders of shares of our common stock, including those shares of our common stock that were issued upon the conversion of our preferred stock in connection with our initial public offering in May 2019 (the "IPO"), are entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are referred to as registrable securities. The holders of these registrable securities possess registration rights pursuant to the terms of our amended and restated investors' rights agreement and are described in additional detail below. The registration of shares of our common stock pursuant to the exercise of the registration rights described below would enable the holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions and limitations, to limit the number of shares the holders may include. The demand, piggyback and Form S-3 registration rights described below will expire no later than three years after the completion of the IPO, or with respect to any particular holder, at such time that such holder can sell its shares under Rule 144 of the Securities Act during any three-month period.

Anti-Takeover Provisions of Delaware Law and Our Charter Documents

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years after the date that such stockholder became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (i) by persons who are directors and also officers and (ii) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least $66^{2}/_{3}\%$ of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 defines a "business combination" to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and

- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 defines an "interested stockholder" as an entity or person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

The statute could prohibit or delay mergers or other takeover or change in control attempts and, accordingly, may discourage attempts to acquire us even though such a transaction may offer our stockholders the opportunity to sell their stock at a price above the prevailing market price.

Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws

Among other things, our amended and restated certificate of incorporation and amended and restated bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate, including the right to approve an acquisition or other change in control;
- provide that the authorized number of directors may be changed only by resolution of our board of directors;
- provide that our board of directors be classified into three classes of directors;
- provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed for cause, which removal may be effected, subject to any limitation imposed by law, by the holders of at least a majority of the voting power of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent or electronic transmission;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- provide that special meetings of our stockholders may be called only by the chairman of our board of directors, our chief executive officer or president or by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- not provide for cumulative voting rights, therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose.

The amendment of any of these provisions would require approval by the holders of at least $66^{2}/_{3}\%$ of the voting power of all of our then-outstanding common stock entitled to vote generally in the election of directors, voting together as a single class.

The combination of these provisions make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Because our board of directors has the power to retain and discharge our officers, these provisions could also make it more

difficult for existing stockholders or another party to effect a change in management. In addition, the authorization of undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change our control.

These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and its policies and to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to reduce our vulnerability to hostile takeovers and to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and may have the effect of delaying changes in our control or management. As a consequence, these provisions may also inhibit fluctuations in the market price of our stock that could result from actual or rumored takeover attempts. We believe that the benefits of these provisions, including increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company, outweigh the disadvantages of discouraging takeover proposals, because negotiation of takeover proposals could result in an improvement of their terms.

Choice of Forum

Our amended and restated certificate of incorporation provides that, with respect to any state actions or proceedings under Delaware statutory or common law, 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 certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable.

Listing

Our common stock is listed on The Nasdaq Global Market under the trading symbol "APLT."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

APPLIED THERAPEUTICS INC.

March 9, 2020

Dear Shoshana:

This letter agreement (the "**Agreement**") sets forth the terms and conditions of your continued full time employment with Applied Therapeutics Inc. (the "**Company**"), effective as of March 9, 2020 (the "**Effective Date**").

1. Employment by the Company.

(a) Position. You will continue to serve as the Company's Chief Executive Officer ("**CEO**") and Chair of the Company's Board of Directors (the "**Board**"). During the term of your employment with the Company, you will devote your best efforts and substantially all of your business time and attention to the business of the Company, except for approved vacation periods and reasonable periods of illness or other incapacities permitted by the Company's general employment policies.

(b) Duties and Location. You will have the duties, responsibilities and authorities as are customary for the position of CEO and as may be reasonably directed by the Board, to which you will report. Your primary work location will be the Company's office in New York, New York. Notwithstanding the foregoing, the Company reserves the right to reasonably require you to perform your duties at places other than your primary office location from time to time, and to require reasonable business travel. The Company may modify your job title and duties as it deems necessary and appropriate in light of the Company's needs and interests from time to time.

2. Base Salary and Employee Benefits.

(a) Salary. You will continue to receive a base salary paid at the rate of $577,500 per year, less standard payroll deductions and tax withholdings. Your base salary will be paid on the Company's ordinary payroll cycle. The base salary will be reviewed annually and may be increased but not decreased, unless in connection with an across-the-board reduction in salary of other similarly situated Company executives.

(b) Benefits. As a regular full-time employee, you will continue to be eligible to participate in the Company's standard employee benefits offered to executive level employees, as in effect from time to time and subject to plan terms and generally applicable Company policies. Details about these benefits plans will be provided, upon request.

3. Annual Bonus. You will be eligible to earn an annual performance and retention bonus of up to fifty percent (50%) of your base salary rate (the "Annual Bonus"). The Annual Bonus

will be based upon the Board assessment of your performance and the Company's attainment of written targeted goals as set by the Board in its sole discretion. Bonus payments, if any, will be subject to applicable payroll deductions and withholdings. Following the close of each calendar year, the Board will determine whether you have earned an Annual Bonus, and the amount of any such bonus, based on the achievement of such goals. No amount of Annual Bonus is guaranteed, and you must be an employee on the Annual Bonus payment date to be eligible to receive an Annual Bonus. The Annual Bonus, if earned, will be paid no later than March 15 of the calendar year after the applicable bonus year. Your bonus eligibility is subject to change in the discretion of the Board (or any authorized committee thereof).

4. **Expenses**. The Company will reimburse you for reasonable travel, entertainment or other expenses incurred by you in furtherance or in connection with the performance of your duties hereunder, in accordance with the Company's expense reimbursement policy as in effect from time to time.

5. **Equity Compensation**. You will continue to be eligible to participate in the Company's equity compensation program, pursuant to which the Company may grant you stock options, restricted stock units, other equity-based awards or a combination thereof ("**Equity Awards**") in respect of shares of the Company's common stock ("**Shares**") pursuant to the Company's 2019 Equity Incentive Plan (the "**Plan**"). The Equity Awards will be subject to all of the terms and conditions set forth in the Plan (or any successor thereto, as applicable) and the applicable award agreement(s) or grant notice(s) covering the Equity Awards. Notwithstanding anything in this Agreement, any equity plan of the Company or any award agreement to the contrary, in the event of a Change in Control (as defined in the Plan), the Company shall accelerate the vesting of any then-unvested Shares subject to your outstanding equity awards such that one hundred percent (100%) of such Shares shall be deemed immediately vested (and exercisable, as applicable) as of the date of such Change in Control.

6. **Compliance with Confidentiality Information Agreement and Company Policies**. In connection with your continued employment with the Company, you will receive and have access to Company confidential information and trade secrets. Accordingly, and also in exchange for the eligibility for the Severance Benefits offered herein, you acknowledge and agree that you have previously executed and will continue to be subject to the Company's Employee Confidential Information, Inventions, Non-Solicitation and Non-Competition Agreement (the "Confidentiality Agreement"), which contains restrictive covenants and prohibits unauthorized use or disclosure of the Company's confidential information and trade secrets, among other obligations. In addition, you are required to abide by the Company's policies and procedures, as modified from time to time within the Company's discretion. In the event the terms of this Agreement differ from or are in conflict with the Company's general employment policies or practices, this Agreement shall control. Notwithstanding anything to the contrary in this Agreement or in the Confidentiality Agreement, Confidential Information shall not include your business contacts prior to your employment with the Company, whether in paper or electronic form (your "Rolodex"); *provided*, *however* that the contents of the Rolodex does not contain proprietary information developed during your employment with the Company or

otherwise belonging to the Company. Additionally, nothing herein is intended to limit the scope of your non-solicitation obligations as set forth in the Confidentiality Agreement.

7. **Protection of Third-Party Information**. In your work for the Company, you will continue to be expected not to make any unauthorized use or disclosure of any confidential or proprietary information, including trade secrets, of any former employer or other third party to whom you have contractual obligations to protect such information. Rather, you will be expected to use only that information which is generally known and used by persons with training and experience comparable to your own, which is common knowledge in the industry or otherwise legally in the public domain, or which is otherwise provided or developed by the Company. You represent that you are able to perform your job duties within these guidelines, and you are not in unauthorized possession of any unpublished documents, materials, electronically-recorded information, or other property belonging to any former employer or other third party to whom you have a contractual obligation to protect such property. In addition, you represent and warrant that your employment by the Company will not conflict with any prior employment or consulting agreement or other agreement with any third party, that you will perform your duties to the Company without violating any such agreement(s), and that you have disclosed to the Company in writing any contract you have signed that may restrict your activities on behalf of the Company.

8. **At-Will Employment Relationship**. Your employment relationship with the Company will continue to be at-will. Accordingly, you may terminate your employment with the Company at any time and for any reason whatsoever simply by notifying the Company; and the Company may terminate your employment at any time, with or without Cause or advance notice. If your employment ends for any reason, the Company will provide you with (i) your unpaid Base Salary through the date of termination; (ii) all of your accrued, but unused paid time off time if required by law or Company policy; and (iii) any unpaid expense reimbursements accrued by you as of the date of termination (the "Accrued Obligations").

9. **Severance Benefits**; **Termination without Cause or Resignation for Good Reason**. If the Company terminates your employment without Cause (including as a result of your death or disability) or you resign for Good Reason (either a termination referred to as a "Qualifying Termination"), and provided such Qualifying Termination constitutes a Separation from Service (as defined under Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder, a "Separation from Service" and the date of such Separation from Service, the "**Separation from Service Date**"), then subject to Sections 11 ("Conditions to Receipt of Severance Benefits") and 12 ("Return of Company Property") below and your continued compliance with the terms of this Agreement (including without limitation the Confidentiality Agreement), in addition to your Accrued Obligations, the Company will provide you (or your estate, as applicable) with the following severance benefits (the "Severance Benefits"):

(a) **Cash Severance**. The Company will pay you (or your estate, as applicable), as cash severance, twelve (12) months of your base salary in effect as of your Separation from Service Date, ignoring any decrease that forms the basis of your resignation for Good Reason, if applicable (such twelve (12) month period the "**Salary**

Continuation Period"), less standard payroll deductions and tax withholdings (the "**Severance**"). The Severance will be paid in installments in the form of continuation of your base salary payments, paid on the Company's ordinary payroll dates, commencing on the Company's first regular payroll date that is more than sixty (60) days following your Separation from Service Date, and shall be for any accrued base salary for the sixty (60)-day period plus the period from the sixtieth (60th) day until the regular payroll date, if applicable, and all salary continuation payments thereafter, if any, shall be made on the Company's regular payroll dates.

(b) **Bonus Severance Payment**. The Company will pay you (or your estate, as applicable) a lump sum cash amount equivalent to your target Annual Bonus for the year in which the Separation from Service Date occurs (the "**Bonus Severance Payment**"). Your base salary as in effect on the Separation from Service Date, ignoring any decrease that forms the basis of your resignation for Good Reason, if applicable, shall be used for calculating the Bonus Severance Payment. The Bonus Severance Payment will be paid within sixty (60) days of the effective date of the Release (namely, the date it can no longer be revoked) but in no event later than March 15th of the year following the year in which the Separation from Service Date occurs.

(c) **COBRA Severance**. As an additional Severance Benefit, the Company will continue to pay the cost of your (and, if applicable, your covered dependents') health care coverage in effect at the time of your Separation from Service for a maximum of twelve (12) months, either under the Company's regular health plan (if permitted), or by paying your COBRA premiums (the "**COBRA Severance**"). The Company's obligation to pay the COBRA Severance on your behalf will cease if you obtain health care coverage from another source (e.g., a new employer or spouse's benefit plan), unless otherwise prohibited by applicable law. You must notify the Company within two (2) weeks if you obtain coverage from a new source. This payment of COBRA Severance by the Company would not expand or extend the maximum period of COBRA coverage to which you would otherwise be entitled under applicable law. Notwithstanding the above, if the Company determines in its sole discretion that it cannot provide the foregoing COBRA Severance without potentially violating applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof provide to you a taxable monthly payment in an amount equal to the monthly COBRA premium that you would be required to pay to continue your group health coverage in effect on the date of your termination (which amount shall be based on the premium for the first month of COBRA coverage), which payments shall be made on the last day of each month regardless of whether you elect COBRA continuation coverage and shall end on the earlier of (x) the date upon which you obtain other coverage or (y) the last day of the twelfth (12th) calendar month following your Separation from Service Date.

(d) **Accelerated Vesting**. The Company also shall accelerate the vesting of any then-unvested shares subject to any outstanding option to purchase shares of the Company's Common Stock such that one hundred percent (100%) of such shares

shall be deemed immediately vested and exercisable as of your Separation from Service Date.

10. **Resignation Without Good Reason; Termination for Cause**. If, at any time, you resign your employment without Good Reason, or the Company terminates your employment for Cause, you will receive only your Accrued Obligations. Under these circumstances, you will not be entitled to any other form of compensation from the Company, including any Severance Benefits, other than your rights to the vested portion of your Option and any other rights to which you are entitled under the Company's benefit programs.

11. **Conditions to Receipt of Severance Benefits**. Prior to and as a condition to your (or your estate's, as applicable) receipt of the Severance Benefits described above, you (or your estate, as applicable) shall execute and deliver to the Company an executive release of claims in favor of and in a form that is customary for similarly situated executives and reasonably acceptable to the Company (the "Release") within the timeframe set forth therein, but not later than forty-five (45) days following your Separation from Service Date, and allow the Release to become effective according to its terms (by not invoking any legal right to revoke it) within any applicable time period set forth therein (such latest permitted effective date, the "Release Deadline").

12. **Return of Company Property**. Upon the termination of your employment for any reason, as a precondition to your receipt of the Severance Benefits (if applicable), within five (5) days after your Separation from Service Date (or earlier if requested by the Company), you will return to the Company all Company documents (and all copies thereof) and other Company property within your possession, custody or control, including, but not limited to, Company files, notes, financial and operational information, customer lists and contact information, product and services information, research and development information, drawings, records, plans, forecasts, reports, payroll information, spreadsheets, studies, analyses, compilations of data, proposals, agreements, sales and marketing information, personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, but not limited to, computers, facsimile machines, mobile telephones, tablets, handheld devices, and servers), credit cards, entry cards, identification badges and keys, and any materials of any kind which contain or embody any proprietary or confidential information of the Company, and all reproductions thereof in whole or in part and in any medium. You further agree that you will make a diligent search to locate any such documents, property and information and return them to the Company within the timeframe provided above. In addition, if you have used any personally-owned computer, server, or e-mail system to receive, store, review, prepare or transmit any confidential or proprietary data, materials or information of the Company, then within five (5) days after your Separation from Service Date you must provide the Company with a computer-useable copy of such information and permanently delete and expunge such confidential or proprietary information from those systems without retaining any reproductions (in whole or in part); and you agree to provide the Company access to your system, as requested, to verify that the necessary copying and deletion is done. If requested, you shall deliver to the Company a signed statement certifying compliance with this Section prior to the receipt of the Severance Benefits. Notwithstanding anything to the contrary herein or in the Confidentiality Agreement, you

shall be entitled to keep copies of your Rolodex (subject to the clarification in the last two sentences of Section 6 herein), and documents relating to your compensation and the terms of your employment with the Company.

13. **Outside Activities**. Throughout your employment with the Company, you may be eligible to engage in civic, educational, not-for-profit or similar types of activities and/or managing your and your family's personal investments and affairs, so long as such activities do not interfere with the performance of your duties hereunder and are in accordance with the Company's Code of Business Conduct and Ethics. During your employment by the Company, except on behalf of the Company, you will not directly or indirectly serve as an officer, director, stockholder, employee, partner, proprietor, investor, joint venturer, associate, representative or consultant of any other person, corporation, firm, partnership or other entity whatsoever known by you to compete with the Company (or is planning or preparing to compete with the Company), anywhere in the world, in any line of business engaged in (or demonstrably planned to be engaged in) by the Company; provided, however, that you may purchase or otherwise acquire up to (but not more than) one percent (1%) of any class of securities of any enterprise (but without participating in the activities of such enterprise) if such securities are listed on any national or regional securities exchange.

14. **Definitions**. For purposes of this Agreement, the following terms shall have the following meanings:

For purposes of this Agreement, "**Cause**" for termination will mean your: (a) conviction (including a guilty plea or plea of nolo contendere) of any felony or any other crime involving fraud, dishonesty or moral turpitude; (b) your commission or attempted commission of or participation in a fraud or act of material dishonesty or misrepresentation against the Company; (c) material breach of your duties to the Company; (d) intentional damage to any property of the Company; (e) willful misconduct, or other willful violation of Company policy that causes material harm to the Company; or (f) material violation of any written and fully executed contract or agreement between you and the Company, including without limitation, material breach of your Confidentiality Agreement, or of any statutory duty you owe to the Company. No Cause shall exist unless the Company has provided you with written notice of termination describing the particular circumstances giving rise to Cause (which notice shall be delivered within thirty (30) days of the initial occurrence or discovery by the Company of the alleged Cause conduct), and has provided you the opportunity to cure, to the extent reasonably susceptible to cure, such circumstances within thirty (30) days after receiving such notice. If you so effect a cure, the notice of Cause shall be deemed rescinded and of no force or effect.

For purposes of this Agreement, you shall have "**Good Reason**" for resigning from employment with the Company if any of the following actions are taken by the Company without your prior written consent: (a) a material reduction in your base salary, which the parties agree is a reduction of at least ten percent (10%) of your base salary (unless pursuant to a salary reduction program applicable generally to the Company's similarly situated employees); (b) a material reduction in your duties, responsibilities and/or authorities, including any material reduction of your duties, responsibilities and/or authorities as a

member of the Board (which, for the avoidance of doubt, shall include any involuntary demotion from your role as Chair of the Board); (c) relocation of your principal place of employment to a place that increases your one-way commute by more than fifty (50) miles as compared to your then-current principal place of employment immediately prior to such relocation; or (d) a material breach of this Agreement. In order to resign for Good Reason, you must provide written notice to the Company's CEO within thirty (30) days after the first occurrence of the event giving rise to Good Reason setting forth the basis for your resignation, allow the Company at least thirty (30) days from receipt of such written notice to cure such event, and if such event is not reasonably cured within such period, you must resign from all positions you then hold with the Company not later than thirty (30) days after the expiration of the cure period.

15. **Compliance with Section 409A**. It is intended that the Severance Benefits set forth in this Agreement satisfy, to the greatest extent possible, the exemptions from the application of Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") (Section 409A, together with any state law of similar effect, "Section 409A") provided under Treasury Regulations 1.409A-1(b)(4), 1.409A-1(b)(5) and 1.409A-1(b)(9). For purposes of Section 409A (including, without limitation, for purposes of Treasury Regulations 1.409A-2(b)(2)(iii)), your right to receive any installment payments under this Agreement (whether severance payments, reimbursements or otherwise) shall be treated as a right to receive a series of separate payments and, accordingly, each installment payment hereunder shall at all times be considered a separate and distinct payment. Notwithstanding any provision to the contrary in this Agreement, if the Company (or, if applicable, the successor entity thereto) determines that the Severance Benefits constitute "deferred compensation" under Section 409A and you are, on the date of your Separation from Service, a "specified employee" of the Company or any successor entity thereto, as such term is defined in Section 409A(a)(2)(B)(i) of the Code (a "Specified Employee"), then, solely to the extent necessary to avoid the incurrence of adverse personal tax consequences under Section 409A, the timing of the Severance Benefits shall be delayed until the earliest of: (i) the date that is six (6) months and one (1) day after your Separation from Service Date, (ii) the date of your death, or (iii) such earlier date as permitted under Section 409A without the imposition of adverse taxation. Upon the first business day following the expiration of such applicable Code Section 409A(a)(2)(B)(i) period, all payments or benefits deferred pursuant to this Section shall be paid in a lump sum or provided in full by the Company (or the successor entity thereto, as applicable), and any remaining payments due shall be paid as otherwise provided herein. No interest shall be due on any amounts so deferred. If the Severance Benefits are not covered by one or more exemptions from the application of Section 409A and the Release could become effective in the calendar year following the calendar year in which you have a Separation from Service, the Release will not be deemed effective any earlier than the Release Deadline. The Severance Benefits are intended to qualify for an exemption from application of Section 409A or comply with its requirements to the extent necessary to avoid adverse personal tax consequences under Section 409A, and any ambiguities herein shall be interpreted accordingly. Notwithstanding anything to the contrary herein, to the extent required to comply with Section 409A, a termination of employment shall not be deemed to have occurred for purposes of any provision of this Agreement providing for the payment of amounts or benefits upon or following a termination of employment unless such termination is also a "separation from service"

within the meaning of Section 409A. With respect to reimbursements or in-kind benefits provided to you hereunder (or otherwise) that are not exempt from Section 409A, the following rules shall apply: (i) the amount of expenses eligible for reimbursement, or in-kind benefits provided, during any one of your taxable years shall not affect the expenses eligible for reimbursement, or in-kind benefit to be provided in any other taxable year, (ii) in the case of any reimbursements of eligible expenses, reimbursement shall be made on or before the last day of your taxable year following the taxable year in which the expense was incurred, (iii) the right to reimbursement or in-kind benefits shall not be subject to liquidation or exchange for another benefit.

16. Section 280G; Parachute Payments.

(a) If any payment or benefit you will or may receive from the Company or otherwise (a "**280G Payment**") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "**Excise Tax**"), then any such 280G Payment provided pursuant to this Agreement (a "**Payment**") shall be equal to the Reduced Amount. The "Reduced Amount" shall be either (x) the largest portion of the Payment that would result in no portion of the Payment (after reduction) being subject to the Excise Tax or (y) the largest portion, up to and including the total, of the Payment, whichever amount (i.e., the amount determined by clause (x) or by clause (y)), after taking into account all applicable federal, state and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in your receipt, on an after-tax basis, of the greater economic benefit notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in a Payment is required pursuant to the preceding sentence and the Reduced Amount is determined pursuant to clause (x) of the preceding sentence, the reduction shall occur in the manner (the "**Reduction Method**") that results in the greatest economic benefit for you. If more than one method of reduction will result in the same economic benefit, the items so reduced will be reduced pro rata (the "**Pro Rata Reduction Method**").

(b) Notwithstanding any provision of subsection (a) above to the contrary, if the Reduction Method or the Pro Rata Reduction Method would result in any portion of the Payment being subject to taxes pursuant to Section 409A that would not otherwise be subject to taxes pursuant to Section 409A, then the Reduction Method and/or the Pro Rata Reduction Method, as the case may be, shall be modified so as to avoid the imposition of taxes pursuant to Section 409A as follows: (A) as a first priority, the modification shall preserve to the greatest extent possible, the greatest economic benefit for you as determined on an after-tax basis; (B) as a second priority, Payments that are contingent on future events (e.g., being terminated without Cause), shall be reduced (or eliminated) before Payments that are not contingent on future events; and (C) as a third priority, Payments that are "deferred compensation" within the meaning of Section 409A shall be reduced (or eliminated) before Payments that are not deferred compensation within the meaning of Section 409A.

(c) Unless you and the Company agree on an alternative accounting firm or law firm, the accounting firm engaged by the Company for general tax compliance purposes as of the day prior to the effective date of the Change in Control transaction shall perform the foregoing calculations. If the accounting firm so engaged by the Company is serving as accountant or auditor for the individual, entity or group effecting the change in control transaction, the Company shall appoint a nationally recognized accounting or law firm to make the determinations required by this Section 16 ("**Section 280G; Parachute Payments**"). The Company shall bear all expenses with respect to the determinations by such accounting or law firm required to be made hereunder. The Company shall use commercially reasonable efforts to cause the accounting or law firm engaged to make the determinations hereunder to provide its calculations, together with detailed supporting documentation, to you and the Company within fifteen (15) calendar days after the date on which your right to a 280G Payment becomes reasonably likely to occur (if requested at that time by you or the Company) or such other time as requested by you or the Company.

(d) If you receive a Payment for which the Reduced Amount was determined pursuant to clause (x) of Section 16(a) and the Internal Revenue Service determines thereafter that some portion of the Payment is subject to the Excise Tax, you agree to promptly return to the Company a sufficient amount of the Payment (after reduction pursuant to clause (x) of Section 16(a)) so that no portion of the remaining Payment is subject to the Excise Tax. For the avoidance of doubt, if the Reduced Amount was determined pursuant to clause (y) of Section 16(a), you shall have no obligation to return any portion of the Payment pursuant to the preceding sentence.

17. **Dispute Resolution**. To ensure the rapid and economical resolution of disputes that may arise in connection with your employment with the Company, you and the Company agree that any and all disputes, claims, or causes of action, in law or equity, including but not limited to statutory claims, arising from or relating to the enforcement, breach, performance, or interpretation of this Agreement, your employment with the Company, or the termination of your employment, shall be resolved pursuant to the Federal Arbitration Act, 9 U.S.C. § 1-16, to the fullest extent permitted by law, by final, binding and confidential arbitration conducted by JAMS or its successor, under JAMS' then applicable rules and procedures for employment disputes before a single arbitrator (available upon request and also currently available at http://www.jamsadr.com/rules-employment-arbitration/). **You acknowledge that by agreeing to this arbitration procedure, both you and the Company waive the right to resolve any such dispute through a trial by jury or judge or administrative proceeding**. Prior to any arbitration, you and the Company agree first to engage in prompt and serious good faith discussions to resolve the dispute. In addition, all claims, disputes, or causes of action under this section, whether by you or the Company, must be brought in an individual capacity, and shall not be brought as a plaintiff (or claimant) or class member in any purported class or representative proceeding, nor joined or consolidated with the claims of any other person or entity. The arbitrator may not consolidate the claims of more than one person or entity, and may not preside over any form of representative or class proceeding. To the extent that the preceding sentences regarding class claims or proceedings are found to violate applicable

law or are otherwise found unenforceable, any claim(s) alleged or brought on behalf of a class shall proceed in a court of law rather than by arbitration. This paragraph shall not apply to any action or claim that cannot be subject to mandatory arbitration as a matter of law, including, without limitation, sexual harassment claims, to the extent such claims are not permitted by applicable law to be submitted to mandatory arbitration (collectively, the "Excluded Claims"). In the event you intend to bring multiple claims, including one of the Excluded Claims listed above, the Excluded Claims may be publicly filed with a court, while any other claims will remain subject to mandatory arbitration. You will have the right to be represented by legal counsel at any arbitration proceeding. Questions of whether a claim is subject to arbitration under this agreement shall be decided by the arbitrator. Likewise, procedural questions which grow out of the dispute and bear on the final disposition are also matters for the arbitrator. The arbitrator shall: (a) have the authority to compel adequate discovery for the resolution of the dispute and to award such relief as would otherwise be permitted by law; and (b) issue a written statement signed by the arbitrator regarding the disposition of each claim and the relief, if any, awarded as to each claim, the reasons for the award, and the arbitrator's essential findings and conclusions on which the award is based. The arbitrator shall be authorized to award all relief that you or the Company would be entitled to seek in a court of law. You and the Company shall equally share all JAMS' arbitration fees. Each party is responsible for its own attorneys' fees, except as expressly set forth in your Confidentiality Agreement. Nothing in this Agreement is intended to prevent either you or the Company from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration. Any awards or orders in such arbitrations may be entered and enforced as judgments in the federal and state courts of any competent jurisdiction.

18. **Indemnification**. You will be entitled to indemnification to the maximum extent permitted by applicable law and the Company's Bylaws with terms no less favorable than provided to any other Company executive officer or director and subject to the terms of any separate written indemnification agreement. At all times during your employment, the Company shall maintain in effect a directors and officers liability insurance policy with you as a covered officer.

19. **Miscellaneous**. This Agreement, together with your Confidentiality Agreement, forms the complete and exclusive statement of your employment agreement with the Company. It supersedes any other agreements or promises made to you by anyone, whether oral or written, including the Offer Letter. Changes in your employment terms, other than those changes expressly reserved to the Company's or Board's discretion in this Agreement, require a written modification approved by you and the Company and signed by you and a duly authorized officer of the Company. This Agreement will bind the heirs, personal representatives, successors and assigns of both you and the Company, and inure to the benefit of both you and the Company, their heirs, successors and assigns. If any provision of this Agreement is determined to be invalid or unenforceable, in whole or in part, this determination shall not affect any other provision of this Agreement and the provision in question shall be modified so as to be rendered enforceable in a manner consistent with the intent of the parties insofar as possible under applicable law. This Agreement shall be construed and enforced in accordance with the laws of the State of New York without regard to conflicts of law principles. Any ambiguity in this Agreement shall not be

construed against either party as the drafter. Any waiver of a breach of this Agreement, or rights hereunder, shall be in writing and shall not be deemed to be a waiver of any successive breach or rights hereunder. This Agreement may be executed and delivered via facsimile, electronic mail (including pdf or any electronic signature complying with the U.S. federal ESIGN Act of 2000, Uniform Electronic Transactions Act or other applicable law) or other transmission method and shall be deemed to have been duly and validly delivered and be valid and effective for all purposes.

[Signature Page Follows]

This Agreement may be executed in one or more counterparts, each of which shall be deemed to be an original, but all of which together shall constitute one and the same agreement.

Sincerely,

/s/ Mark Vignola
Name: Mark Vignola
Title: Chief Financial Officer

Reviewed, Understood, and Accepted:

/s/ Shoshana Shendelman	March 11, 2020
Shoshana Shendelman	Date

Exhibit 10.14

AMENDMENT TO EMPLOYMENT AGREEMENT

This Amendment to Employment Agreement (this "Amendment") is entered into on March 9, 2020, by and between Riccardo Perfetti ("Executive") and Applied Therapeutics Inc., a Delaware corporation (the "Company"). For purposes of this Amendment, Executive and the Company may collectively be referred to as "the Parties."

WHEREAS, Executive and the Company are parties to an Employment Agreement dated as of August 28, 2019 (the "Agreement") setting forth the terms and conditions of Executive's employment with the Company; and

WHEREAS, the Parties desire to amend the Agreement to provide (i) that a termination of employment due to death or disability shall constitute a Qualifying Termination (as defined in the Agreement) and (ii) for accelerated vesting of Executive's outstanding equity awards in the event of a Change in Control (as defined in the Company's 2019 Equity Incentive Plan).

NOW THEREFORE, in consideration of the mutual covenants and promises made in this Amendment, Executive and the Company hereby agree as follows:

1. The following sentence shall be added to the end of Section 5 of the Agreement:

   "Notwithstanding anything in this Agreement, any equity plan of the Company or any award agreement to the contrary, in the event of a Change in Control (as defined in the Company's 2019 Equity Incentive Plan), the Company shall accelerate the vesting of any then-unvested shares of the Company's Common Stock subject to your outstanding equity awards such that one hundred percent (100%) of such shares shall be deemed immediately vested (and exercisable, as applicable) as of the date of such Change in Control."

2. The first sentence of Section 9 of the Agreement shall be deleted and replaced in its entirety with the below:

   "If the Company terminates your employment without Cause (including as a result of your death or disability) or you resign for Good Reason (either a termination referred to as a "**Qualifying Termination**"), and provided such Qualifying Termination constitutes a Separation from Service (as defined under Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder, a "**Separation from Service**" and the date of such Separation from Service, the "**Separation from Service Date**"), then subject to Sections 11 ("**Conditions to Receipt of Severance Benefits**") and 12 ("**Return of Company Property**") below and your continued compliance with the terms of this Agreement (including without limitation the Confidentiality Agreement), in addition to your Accrued Obligations, the Company will provide you (or your estate, as applicable) with the following severance benefits (the "**Severance Benefits**"):"

3. The first sentence of Section 9(a) of the agreement shall be deleted and replaced in its entirety with the below:

   "The Company will pay you (or your estate, as applicable), as cash severance, twelve (12) months of your base salary in effect as of your Separation from Service Date, less standard payroll deductions and tax withholdings (the "**Severance**")."

4. The first sentence of Section 9(b) of the Agreement shall be deleted and replaced in its entirety with the below:

   "The Company will pay you (or your estate, as applicable) a lump sum cash amount equivalent to your target Annual Bonus for the year in which the Separation from Service Date occurs (the "**Bonus Severance Payment**")."

5. The first sentence of Section 10 of the Agreement shall be deleted and replaced in its entirety with the below:

   "If, at any time, you resign your employment without Good Reason, or the Company terminates your employment for Cause, you will receive only your Accrued Obligations."

6. Section 11 of the Agreement shall be deleted and replaced in its entirety with the below:

   "Conditions to Receipt of Severance Benefits. Prior to and as a condition to your (or your estate's, as applicable) receipt of the Severance Benefits described above, you (or your estate, as applicable) shall execute and deliver to the Company an executive release of claims in favor of and in a form acceptable to the Company (the "Release") within the timeframe set forth therein, but not later than forty-five (45) days following your Separation from Service Date, and allow the Release to become effective according to its terms (by not invoking any legal right to revoke it) within any applicable time period set forth therein (such latest permitted effective date, the "Release Deadline")."

7. Except as set forth herein, the Agreement shall continue in full force and effect in accordance with its terms.

8. This Amendment may be executed simultaneously in two or more counterparts, any one of which need not contain the signatures of more than one party, but all of which counterparts taken together will constitute one and the same agreement.

[Signature Page Follows]

APPLIED THERAPEUTICS INC.

By: /s/ Shoshana Shendelman
Name Shoshana Shendelman
Title: Chief Executive Officer

EXECUTIVE

/s/ Riccardo Perfetti
Riccardo Perfetti

[Signature Page to Amendment to Employment Agreement]

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in Registration Statement on Form S-8 (Form S-8 No. 333-231618) of our report dated March 13, 2020, with respect to the financial statements of Applied Therapeutics, Inc., included in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ Ernst & Young LLP
New York, New York
March 13, 2020

Exhibit 31.1

CERTIFICATIONS

I, Shoshana Shendelman, certify that:

1. I have reviewed this Form 10-K of Applied Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

Date: March 13, 2020

By: /s/ Shoshana Shendelman
Name: Shoshana Shendelman, Ph.D.
Title: Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Mark Vignola, certify that:

1. I have reviewed this Form 10-K of Applied Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

Date: March 13, 2020

By: /s/ Mark Vignola
Name: Mark Vignola, Ph.D.
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Shoshana Shendelman, Chief Executive Officer of Applied Therapeutics, Inc. (the "Company"), hereby certifies that, to the best of her knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 13, 2020

By: /s/ Shoshana Shendelman
Name: Shoshana Shendelman, Ph.D.
Title: Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Mark Vignola, Chief Financial Officer of Applied Therapeutics, Inc. (the "Company"), hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019, to which this Certification is attached as Exhibit 32.2 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

Dated: March 13, 2020

By: /s/ Mark Vignola
Name: Mark Vignola, Ph.D.
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)