Filed Pursuant to Rule 424(b)(4)
Registration No. 333-256949

PROSPECTUS

8,682,142 Shares

Common Stock

We are offering 8,682,142 shares of common stock. This is our initial public offering of our common stock.

Prior to this offering, there has been no public market for our shares. The initial public offering price is $14.00 per share. Our common stock has been approved for listing on The Nasdaq Global Market under the symbol "AVTE".

We are an "emerging growth company" and "smaller reporting company" under the U.S. federal securities laws and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and for future filings.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 10 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of the securities that may be offered under this prospectus, nor have any of these organizations determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public offering price	$ 14.00	$121,549,988
Underwriting discount[1]	$ 0.98	$ 8,508,499
Proceeds, before expenses, to us	$ 13.02	$113,041,489

(1) We refer you to "Underwriting" beginning on page 149 for additional information regarding underwriting compensation.

Delivery of the shares of common stock will be made on or about July 2, 2021.

We have granted the underwriters an option for a period of 30 days to purchase an additional 1,302,321 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $9.8 million, and the total proceeds to us, before expenses, will be $130.0 million.

Joint Book-Running Managers

Jefferies **Cowen** **Evercore ISI**

Lead Manager

Wedbush PacGrow

The date of this prospectus is June 29, 2021.

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Through and including July 24, 2021 (25 days after the commencement of this offering), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

We have not, and the underwriters have not, authorized anyone to provide any information or to make any representation other than those contained in this prospectus, any amendment or supplement to this prospectus or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the shares of common stock offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus, any amendment or supplement to this prospectus or any applicable free writing prospectus is current only as of its date, regardless of its time of delivery or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

The market data and certain other statistical information used throughout this prospectus are based on independent industry publications, governmental publications, reports by market research firms, or other independent sources that we believe to be reliable sources. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this prospectus, and we believe that these sources are reliable; however, we have not independently verified the information contained in such publications. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this prospectus. Some data are also based on our good faith estimates.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus. Unless the context otherwise requires, the terms "Aerovate," "Aerovate Therapeutics," "the Company," "the Registrant," "we," "us," and "our" in this prospectus refer to Aerovate Therapeutics, Inc.

Overview

We are a clinical stage biopharmaceutical company focused on developing drugs that meaningfully improve the lives of patients with rare cardiopulmonary disease. Our initial focus is on advancing AV-101, our dry powder inhaled formulation of imatinib for the treatment of pulmonary arterial hypertension, or PAH, a devastating disease impacting approximately 70,000 people in the United States and Europe. Imatinib, marketed as Gleevec tablets, was originally developed for the treatment of multiple cancers. Oral imatinib also demonstrated statistically significant improvement on the primary endpoint, six-minute walk distance, and multiple secondary hemodynamic endpoints in PAH patients in an international Phase 3 trial conducted by Novartis but was poorly tolerated due to adverse events, or AEs, and never approved for the treatment of PAH. AV-101, delivered using a dry powder inhaler, is designed to provide lung concentrations at or above those observed with the oral dose while limiting systemic levels of the drug. We have completed a Phase 1 study in healthy volunteers and AV-101 was generally well-tolerated with no serious adverse events reported. We anticipate initiating a Phase 2b/3 trial of AV-101 in PAH patients in the second half of 2021, and we have assembled a team with deep expertise in developing innovative PAH and inhaled therapies and commercializing novel drugs.

PAH Overview

PAH is an orphan disease with unmet medical need and is characterized by high pressure in the vessels transporting blood from the right side of the heart to the lungs. This high pressure is caused by abnormal cellular proliferation, which over time results in narrowing of the pulmonary vessels and forces the heart to work harder to pump blood through the lungs. The severe blood flow restriction and strain on the heart becomes increasingly severe over time and ultimately leads to heart failure that is often fatal. We estimate there are between 30,000-40,000 patients treated with approved PAH therapies in the U.S. alone, many of whom are on two or more approved PAH therapies. It is estimated that the combined global sales for PAH products in 2020 was $5.4 billion. Despite the availability of multiple approved therapies, PAH has a five-year life expectancy for newly diagnosed and prevalent patients between 61% and 65%. None of the approved therapies directly address the abnormal cellular proliferation of the pulmonary vasculature that causes the increased resistance to blood flow. We believe that novel treatments that primarily address abnormal cellular proliferation may provide therapeutic benefit to PAH patients and lead to improved quality of life.

Our Approach, AV-101

Our focus on developing AV-101 is driven by historical results from the Phase 3 IMPRES clinical trial of oral imatinib for the treatment of PAH patients. Oral imatinib is a well-characterized targeted kinase inhibitor and approved oncology treatment, but clinical trials also supported its potential for the treatment of PAH. The Phase 3 IMPRES trial was a placebo-controlled clinical trial of oral imatinib, conducted globally by Novartis, in 202 PAH patients whose disease was not adequately controlled by two or all three classes of approved PAH therapies. After 24 weeks of treatment with oral imatinib, patients achieved on average an increase of 32 meters compared to placebo in the distance they could walk in six minutes, a measure known as the 6MWD, and average improvement (reduction) of 32% compared to placebo in pulmonary vascular resistance, a measure known as PVR. However, treatment with oral imatinib was also associated with significant tolerability issues and adverse events, including nausea, edema, diarrhea and vomiting. Patients taking oral imatinib also experienced serious adverse events, the most frequent of which were anemia (7%), worsening of pulmonary hypertension (6%), dyspnea (6%), peripheral edema (6%), presyncope (5%), diarrhea (3%), device-related

infection (3%), subdural hematoma (2%) and syncope (1%). Despite the clinical effects of oral imatinib, 26% of patients on oral imatinib, compared to 7% on placebo, discontinued due to AEs by 24 weeks.

Our company was formed to develop an inhaled formulation of imatinib as a means of delivering therapeutically relevant drug concentrations to the lungs while minimizing systemic and gastrointestinal exposure, which we believe are the sources of the observed intolerability of oral imatinib. We have brought together leaders both in the field of PAH drug development as well as in the area of inhaled drug formulation to invent AV-101, a drug/device combination designed to deliver imatinib directly to the lungs.

We have completed a Phase 1 trial in the United States of AV-101 in 82 healthy adults. Repeat inhaled doses of up to 90 mg were well-tolerated and resulted in systemic plasma levels that were below those observed with the 400 mg oral dose of imatinib (Gleevec) used in the IMPRES trial. In our Phase 1 trial, there were no serious adverse events associated with AV-101. We anticipate initiating a double-blinded, placebo-controlled, randomized Phase 2b/3 trial of AV-101 in the second half of 2021 in PAH patients taking at least two background therapies. Our Phase 2b/3 trial of AV-101 will be conducted globally.

The Phase 2b portion of this trial will enroll approximately 200 PAH patients and is designed to assess safety, tolerability and inform dose selection for the Phase 3 portion using changes in PVR, an objective measure of the effect of AV-101 on hemodynamic function in PAH patients, as the primary endpoint. We will measure 6MWD as a secondary endpoint in the Phase 2b portion of this trial. We anticipate that topline data from the Phase 2b portion of this trial will be available in the middle of 2023.

We are pursuing a clinical development program utilizing established endpoints for development of previous PAH drugs, as well as enrollment criteria and dosing duration previously studied in oral imatinib PAH trials. At our April 14, 2021 end-of-Phase 1 meeting with the Food and Drug Administration, or FDA, we received regulatory guidance that our clinical program could support a New Drug Application, or NDA, submission; however, the process of clinical development is inherently uncertain and there can be no guarantee that we will obtain marketing approval. AV-101 has been granted orphan drug designation by the FDA for the treatment of PAH. We have filed for patent protection of the composition of the aerosol, drug product, manufacturing and methods of use. We retain worldwide commercial rights to AV-101.

Our Team and Investors

Our executive management team has extensive experience in the clinical development and the commercialization of orphan drug indications. Timothy P. Noyes, our Chief Executive Officer, was a senior executive at GelTex Pharmaceuticals, Inc., or GelTex, and Genzyme Corporation, or Genzyme, where he headed all launch planning and the commercialization of Renagel, a treatment for hemodialysis patients that resulted in Genzyme's acquisition of GelTex for more than $1 billion. Benjamin T. Dake, Ph.D., our Founder, President, Chief Operating Officer and Secretary, a cancer biologist, investor and entrepreneur, recognized the potential benefits of developing a lung-targeted imatinib and secured multiple rounds of funding to build the team at Aerovate with experts like Ralph Niven, Ph.D., our Chief Development Officer, who has 25 years of expertise in translational medicine and inhalation dosage forms, and Hunter Gillies, M.B.Ch.B., our Chief Medical Officer, who has led Phase 2 and Phase 3 PAH trials at Pfizer Inc. and Gilead Sciences, Inc. and has designed and executed PAH trials with several smaller biotechnology companies. George A. Eldridge, our Chief Financial Officer, has served as CFO for several biotechnology companies, leading four of these companies to the public markets.

In addition, we are supported by leading life sciences investors, including RA Capital, Sofinnova Investments, Atlas Venture, Cormorant Asset Management, Surveyor Capital (a Citadel company) and Osage Venture Partners.

Our Strategy

Our strategy is to develop and commercialize AV-101 for patients suffering from PAH. Key elements of our strategy include our plans to:

- *Complete regulatory discussions for AV-101 in the United States and Europe*
- *Advance AV-101 through approval*
- *Commercialize AV-101 directly in the United States*

- *Pursue additional indications for AV-101*
- *Expand our pipeline by accessing additional product opportunities*

Recent Developments

On June 4, 2021, upon the completion of the Second Milestone Closing and Third Milestone Closing outlined in the Series A Preferred Stock Purchase Agreement, we sold 29,338,346 shares of Series A redeemable convertible preferred stock at $1.893 per share for aggregate gross proceeds of $55.5 million.

Impact of COVID-19

In March 2020, the World Health Organization declared the outbreak of the coronavirus disease 2019, or COVID-19, pandemic, which continues to spread throughout the United States and worldwide. The ultimate extent of the impact of the COVID-19 pandemic on our business, financial condition and results of operations is highly uncertain and will depend on future developments that cannot be predicted, including new information that may emerge concerning the severity of the COVID-19 pandemic and actions taken by government authorities and businesses to contain or prevent the further spread of COVID-19. For instance, a resurgence or continuation of COVID-19 cases, or the continued identification of new variants of COVID-19, could cause a more widespread or severe impact on commercial activity depending on where infection rates are highest. If we or any of the third parties with whom we engage were to experience any additional shutdowns or other prolonged business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially or negatively affected, which could have a material adverse impact on our business, results of operations and financial condition.

The global COVID-19 pandemic continues to evolve, and we will continue to monitor the COVID-19 situation. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, contract research organizations, or CROs, third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. To the extent possible, we are conducting business as usual, with only necessary or advisable modifications to employee travel. We currently do not lease any facilities as our entire organization works remotely. We plan to lease office space in the greater Boston, Massachusetts metropolitan area. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. At this point, the extent to which the COVID-19 pandemic may affect our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain and is subject to change.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section titled “Risk Factors” in this prospectus. These risks include, among others:

- We are a clinical-stage biopharmaceutical company with a limited operating history.
- We have incurred significant operating losses since our inception and anticipate that we will continue to incur losses for the foreseeable future.
- Our business is entirely dependent on the successful development, regulatory approval and commercialization of AV-101, our only product candidate under development.
- We have only recently begun testing of AV-101, a dry powder formulation of imatinib for the treatment of PAH administered using a dry powder inhaler, to assess its safety and tolerability. Although we believe that AV-101 has therapeutic potential for PAH based on oral imatinib’s results in the Phase 3 IMPRES trial, we are utilizing a novel dry powder formulation which may not achieve better or similar levels of clinical activity or may have similar tolerability challenges as oral imatinib. The results of earlier studies and trials of oral imatinib in PAH patients and our Phase 1 clinical trial of AV-101 may not be predictive of future trial results for AV-101.

- If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- We face, and will continue to face, significant competition and our failure to effectively compete may prevent us from achieving significant market penetration for AV-101, if approved. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete.
- We rely, and intend to continue to rely, on qualified third parties to supply all components of AV-101. As a result, we are dependent on several third parties, some of which are sole source suppliers, for the manufacture of AV-101 and our supply chain, and if we experience problems with any of these suppliers, or they fail to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, it would materially and adversely affect our business.
- We rely, and intend to continue to rely, on third parties in the conduct of all of our clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or meet expected deadlines, we may be unable to obtain regulatory approval for AV-101.
- We may be unable to obtain regulatory approval for AV-101 under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of AV-101 and adversely impact our potential to generate revenue, our business and our results of operations.
- AV-101 is a drug-device combination product, which may result in additional regulatory risks.
- We plan to conduct clinical trials for AV-101 outside the United States, and the FDA, European Medicines Agency, or EMA, and applicable foreign regulatory authorities may not accept data from such trials.
- We have many pending patent applications with respect to AV-101, but do not own any issued patents. We can provide no assurance that any of our current or future patent applications will result in issued patents.
- We will need to increase the size of our organization, and we may experience difficulties in managing growth.
- We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, our business may be materially and adversely affected.
- The COVID-19 pandemic, or a similar pandemic, epidemic or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of AV-101.
- Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Corporate History

We were incorporated under the laws of the State of Delaware in July 2018. Our principal corporate office is located at 200 Berkeley Street, Floor 18, Boston, MA 02116, and our telephone number is (617) 443-2400. Our website address is www.aerovatetx.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols® and™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We qualify as an “emerging growth company” as defined in the Jumpstart Our Business Startups Act of 2012, as amended. As an emerging growth company, we may take advantage of specified reduced disclosure

and other requirements that are otherwise applicable generally to public companies. These provisions include:

- being permitted to only disclose 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;
- reduced disclosure about our executive compensation arrangements;
- not being required to hold advisory votes on executive compensation or to obtain stockholder approval of any golden parachute arrangements not previously approved; and
- an exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions until the fifth anniversary of our initial public offering or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (iv) the last day of the fiscal year in which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter.

THE OFFERING

Common stock offered by us	8,682,142 shares.
Common stock to be outstanding immediately after this offering	23,108,072 shares (24,410,393 shares if the underwriters exercise their option to purchase additional shares in full).
Underwriters' option to purchase additional shares	We have granted the underwriters an option, exercisable for 30 days after the date of this prospectus, to purchase up to 1,302,321 additional shares from us.
Use of proceeds	We estimate that our net proceeds from the sale of shares of our common stock in this offering will be approximately $109.9 million, or $126.9 million if the underwriters exercise in full their option to purchase additional shares, based on the initial public offering price of $14.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to fund further development of AV-101 through the completion of the Phase 2b portion and the data read out of the Phase 3 portion of our global Phase 2b/3 clinical trial, continued chemistry, manufacturing and controls work for AV-101, expenses related to pursing a commercial launch of AV-101 and the remainder, if any, for working capital and general corporate purposes, which may include the hiring of additional personnel, capital expenditures and the costs of operating as a public company. See "Use of Proceeds" for additional information.
Risk factors	You should carefully read the "Risk Factors" section of this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
Nasdaq Global Market symbol	AVTE

The number of shares of our common stock to be outstanding after this offering is based on 14,425,930 shares of our common stock outstanding as of June 22, 2021, which assumes the automatic conversion of all outstanding shares of our convertible preferred stock as of June 22, 2021, and excludes:

- 1,938,954 shares of common stock issuable upon the exercise of stock options outstanding under our 2018 Equity Incentive Plan, or our 2018 Plan, as of June 22, 2021, at a weighted average exercise price of $2.12 per share;
- 832,000 shares of our common stock issuable upon the exercise of stock options granted in connection with this offering under our 2021 Stock Option and Incentive Plan, or our 2021 Plan, which became effective in connection with this offering, to certain of our directors, executive officers, and employees at an exercise price per share equal to the initial public offering price in this offering;
- 1,768,000 additional shares of our common stock that became available for future issuance under our 2021 Plan, as well as any future evergreen increases pursuant to the terms of the 2021 Plan; and
- 230,000 shares of our common stock that became available for future issuance under our Employee Stock Purchase Plan, or our ESPP, which became effective in connection with this offering, as well as any future evergreen increases pursuant to the terms of the ESPP.

Except as otherwise indicated, all information in this prospectus assumes or gives effect to:

- the issuance of 29,338,346 shares of Series A redeemable convertible preferred stock at $1.893 per share since March 31, 2021;
- the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 14,182,854 shares of our common stock immediately prior to the completion of this offering;
- no exercise of the outstanding options described above;
- no exercise by the underwriters of their option to purchase up to an additional 1,302,321 shares of our common stock in this offering;
- a one-for-3.1060103 reverse split of our common stock and a proportional adjustment to the conversion ratio of our convertible preferred stock, which became effective prior to the completion of this offering; and
- the filing of our second amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the completion of this offering.

SUMMARY FINANCIAL DATA

The following tables set forth a summary of our historical financial data as of, and for the periods ended on, the dates indicated. We have derived the summary statements of operations and comprehensive loss data for the years ended December 31, 2019 and 2020 and the summary balance sheet data as of December 31, 2020 from our audited financial statements included elsewhere in this prospectus. The statement of operations and comprehensive loss data for the three months ended March 31, 2020 and 2021 and the balance sheet data as of March 31, 2021 have been derived from our unaudited interim condensed financial statements appearing at the end of this prospectus and have been prepared on the same basis as the audited financial statements. You should read these data together with our financial statements and related notes included elsewhere in this prospectus and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations". Our historical results for any prior period are not necessarily indicative of our future results.

	YEAR ENDED DECEMEBER 31,		THREE MONTHS ENDED MARCH 31,	
	2019	2020	2020	2021
	(in thousands, except share and per share amounts)		(unaudited)	
Statements of Operations and Comprehensive Loss Data:				
Operating expenses:				
Research and development	$ 3,112	$ 7,940	$ 1,206	$ 2,196
General and administrative	218	949	152	584
Total operating expensess	3,330	8,889	1,358	2,780
Provision for income taxes	1	—	—	—
Loss from operations	(3,331)	(8,889)	(1,358)	(2,780)
Other income (expense), net	1	(722)	(78)	(1)
Net loss and comprehensive loss	$ (3,330)	$ (9,611)	$ (1,436)	$ (2,781)
Net loss per share, basic and diluted[1][3]	$ (13.79)	$ (40.31)	$ (5.95)	$ (11.49)
Weighted-average shares of common stock outstanding, basic and diluted[1][3]	241,467	242,232	241,467	243,076
Pro forma net loss per share, basic and diluted[2][3]		$ (4.11)		$ (0.62)
Pro forma weighted-average shares of common stock outstanding, basic and diluted[2][3]		2,374,927		4,496,704

(1) See Note 1 to our audited financial statements and Note 1 to our unaudited interim condensed financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

(2) Pro forma basic and diluted net loss per share is calculated to give effect to the one-for-one conversion of all outstanding shares of our convertible preferred stock into shares of our common stock using the as-converted method as though the conversion had occurred as of the beginning of the period presented or the date of issuance, if later.

(3) Reflects a 1-for-3.1060103 reverse stock split of our common stock, which became effective prior to the completion of this offering.

	AS OF MARCH 31, 2021		
	ACTUAL	PRO FORMA[1]	PRO FORMA AS ADJUSTED[2]
		(in thousands) (unaudited)	
Balance Sheet Data:			
Cash	$ 8,641	$ 64,178	$ 174,085
Working capital[3]	7,822	63,359	173,266
Total assets	9,948	65,485	175,085
Total liabilities	1,782	1,782	1,782
Convertible preferred stock	24,281	—	—
Total accumulated deficit	(16,201)	(16,201)	(16,201)
Total shareholders' (deficit) equity	(16,115)	63,703	173,610

(1) The pro forma balance sheet data gives effect to: (i) the issuance of 29,338,346 shares of Series A redeemable convertible preferred stock at $1.893 per share since March 31, 2021, (ii) the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 14,182,854 shares of our common stock and the related reclassification of the carrying value of the convertible preferred stock to permanent equity immediately prior to the closing of this offering, as if such conversion had occurred on March 31, 2021; and (iii) the filing and effectiveness of our amended and restated certificate of incorporation, which will be in effect immediately prior to the closing of this offering.

(2) The pro forma as adjusted balance sheet data gives effect to (i) the pro forma adjustments set forth in footnote (1) above, and (ii) the issuance and sale of 8,682,142 shares of our common stock in this offering at the initial public offering price of $14.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

(3) We define working capital as current assets less current liabilities. See our financial statements included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this prospectus, including our financial statements and the related notes and "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.

Risks Related to Our Limited Operating History, Financial Position, and Capital Requirements

We are a clinical-stage biopharmaceutical company with a limited operating history.

We are a clinical-stage biopharmaceutical company established in July 2018 with a limited operating history. Since our inception, we have devoted substantially all of our efforts to organizing and staffing our company, research and development of AV-101, our initial product candidate, business planning, raising capital, and providing general and administrative support for these operations. We have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry. We have completed our Phase 1 clinical trial of AV-101 for a pulmonary arterial hypertension, or PAH, indication. We plan to initiate our Phase 2b/3 clinical trial for AV-101 in PAH patients in the second half of 2021. We may explore additional indications for AV-101, but do not intend to conduct research on additional product candidates at this time. We have no products approved for commercial sale and therefore have never generated any revenue from product sales, and we do not expect to in the foreseeable future. We have no other experience as a company conducting clinical trials, submitting applications for regulatory approvals, such as a new drug application, or NDA, or commercializing any products.

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

We have incurred significant operating losses in each year since our incorporation in July 2018, do not expect to become profitable in the near future, and may never achieve profitability. Our net losses were $3.3 million and $9.6 million for the years ended December 31, 2019 and 2020, respectively, and $1.4 million and $2.8 million for the three months ended March 31, 2020 and 2021, respectively. As of December 31, 2020 and March 31, 2021, we had an accumulated deficit of $13.4 million and $16.2 million, respectively. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We have no products approved for commercial sale, have not generated any revenue from product sales and have incurred losses in each year since our inception in July 2018. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development program of AV-101 and from general and administrative costs associated with our operations. AV-101 will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We also do not yet have a sales organization or commercial infrastructure and, accordingly, we will incur significant expenses to develop a sales organization or commercial infrastructure in advance of generating any commercial product sales. In addition, once we are a public company, we will incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant expenses and operating losses for the foreseeable future, and we anticipate these losses will increase as we continue to develop AV-101 through clinical trials and regulatory submissions. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the extent of any future losses or when we will become profitable, if at all. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital.

The amount of our future losses is uncertain and our quarterly and annual operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline. Our quarterly and annual operating results may fluctuate significantly

in the future due to a variety of factors, many of which are outside of our control and may be difficult to predict, including the following:

- the timing and success or failure of the clinical development of AV-101, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- our ability to successfully open clinical trial sites for AV-101 and recruit and retain subjects for clinical trials, and any delays caused by difficulties in such efforts;
- our ability to obtain regulatory approval for AV-101, and the timing and scope of any such approvals we may receive;
- the timing and cost of, and level of investment in, research and development activities relating to AV-101, which may change from time to time;
- the cost of manufacturing AV-101, should it receive regulatory approval, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- the experience of any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues or other regulatory challenges;
- our ability to attract, hire and retain qualified personnel;
- the establishment of a sales, marketing and distribution infrastructure and the scaling-up manufacturing capabilities, whether alone or with third parties, to commercialize any product candidates for which we may obtain regulatory approval, if any;
- expenditures that we will or may incur to pursue additional indications for AV-101 or develop or acquire additional product candidates;
- the level of demand for AV-101 should it receive regulatory approval, which may vary significantly;
- the risk/benefit profile, cost and reimbursement policies with respect to AV-101, if approved, and existing and potential future therapeutics that compete with AV-101;
- the changing and volatile United States and global economic environments, including as a result of the coronavirus disease 2019, or COVID-19, pandemic; and
- future accounting pronouncements or changes in our accounting policies.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated guidance we may provide.

We have no products approved for commercial sale and have not generated any revenue from product sales.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated revenue, and we do not expect to generate any revenue in the near future. We do not expect to generate significant revenue unless and until we obtain regulatory approval of, and begin to sell AV-101. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully enroll subjects in, and complete, our ongoing and planned clinical trials for AV-101;
- obtain sufficient safety data required to obtain United States and foreign regulatory approval for AV-101;
- timely file and FDA acceptance of our NDA for AV-101 for review;
- receive regulatory approvals from the FDA and foreign regulatory authorities for AV-101 in order to commence marketing of AV-101;
- establish commercial manufacturing capabilities or make arrangements with third-party manufacturers for clinical supply and commercial manufacturing;
- obtain and maintain patent and trade secret protection or regulatory exclusivity for AV-101;

- launch commercial sales of AV-101, if approved, whether alone or in collaboration with others;
- obtain and maintain acceptance of AV-101, if and when approved, by patients, the medical community and third-party payors;
- position AV-101 to effectively compete with other therapies;
- obtain and maintain healthcare coverage and adequate reimbursement;
- enforce and defend intellectual property rights and claims;
- implement measures to help minimize the risk of COVID-19 to our employees as well as patients and subjects enrolled in our clinical trials; and
- maintain a continued acceptable safety profile of AV-101 following approval.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize AV-101, which would materially harm our business. If we do not receive regulatory approvals for AV-101, we may not be able to continue our operations.

Even if we consummate this offering, we will need to raise substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or terminate our product development or commercialization efforts.

Since our inception, we have invested substantially all of our efforts and financial resources in the development of AV-101 to address the core disease processes of PAH. We believe that we will continue to expend substantial resources for the foreseeable future in connection with the clinical development of AV-101, including in connection with our Phase 2b/3 clinical trial. These expenditures will include costs associated with clinical trials, obtaining regulatory approvals, and manufacturing and supply, as well as marketing and selling AV-101, if approved for sale. In addition, other unanticipated costs may arise. Because the outcome of any clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of AV-101.

As of March 31, 2021, we had cash of $8.6 million. In addition, on June 4, 2021, we raised aggregate gross proceeds of $55.5 million from the issuance of shares of our Series A redeemable convertible preferred stock. We believe the net proceeds from this offering, together with our existing cash, will be sufficient to fund our planned operations into early 2025. However, our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned. 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.

Our future capital requirements depend on many factors, including:

- the scope, timing, rate of progress, results and costs of our preclinical studies and clinical trials for AV-101;
- the number and scope of additional product candidates we decide to pursue;
- the extent to which we discover and develop additional product candidates;
- the scope and costs of manufacturing development and commercial manufacturing activities;
- the cost, timing and outcome of regulatory review of AV-101 and any additional product candidates;
- the cost of building a sales force in anticipation of commercialization of AV-101 and any additional product candidates;
- the cost and timing associated with commercializing AV-101 and any additional product candidates, if approved;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- any product liability or other lawsuits related to AV-101 and any additional product candidates;
- our efforts to enhance operational systems and our ability to attract, hire and retain qualified personnel, including personnel to support the development of AV-101 and any additional product candidates;
- the extent to which we pursue additional indications for AV-101;
- the extent to which we acquire or in-license other product candidates;

- our ability to establish and maintain collaborations on favorable terms, if at all;
- the costs associated with being a public company;
- the potential additional expenses attributable to adjusting our development plans (including any supply related matters) to the COVID-19 pandemic; and
- the timing, receipt and amount of sales of AV-101 and any additional product candidates, if approved.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to:

- delay, limit, reduce or terminate clinical studies or other development activities for AV-101; or
- delay, limit, reduce or terminate our efforts to establish manufacturing and sales and marketing capabilities or other activities that may be necessary to commercialize AV-101, or reduce our flexibility in developing or maintaining our sales and marketing strategy.

We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or AV-101 that we would otherwise pursue on our own. We do not expect to realize revenue from sales of AV-101 in the foreseeable future, if at all, and unless and until AV-101 is clinically tested, approved for commercialization and successfully marketed. To date, we have funded our operations through private placements of convertible preferred stock and convertible notes. We will be required to seek additional funding in the future and currently intend to do so through public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources.

If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize AV-101. Disruptions in the financial markets in general and more recently due to the COVID-19 pandemic may make equity and debt financing more difficult to obtain, and may have a material adverse effect on our ability to meet our fundraising needs. We cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all.

Our recurring losses from operations could continue to raise substantial doubt regarding our ability to continue as a going concern. Our ability to continue as a going concern requires that we obtain sufficient funding to finance our operations.

We have incurred significant operating losses since our inception and have never generated product revenue, and it is possible we will never generate product revenue or profit. Meaningful revenues will likely not be available until and unless AV-101 is approved by the FDA or comparable regulatory agencies in other countries and successfully marketed, either by us or a partner, an outcome which may not occur. Accordingly, we have concluded that substantial doubt exists regarding our ability to continue as a going concern. Our audited financial statements appearing at the end of this prospectus have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. These financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of these uncertainties related to our ability to operate on a going concern basis. The audited financial statements as of and for the year ended December 31, 2020 also did not factor in the proceeds received on June 4, 2021 from the Second Milestone Closing and Third Milestone Closing of our Series A redeemable convertible preferred stock, for which we received aggregate gross proceeds of $55.5 million. In its report on our financial statements for the year ended December 31, 2020, our independent registered public accounting firm included an explanatory paragraph stating that our recurring losses from operations and net capital deficiency raise substantial doubt about our ability to continue as a going concern. In our unaudited condensed financial

statements for March 31, 2021, after considering the additional proceeds from our milestone closings and existing cash on-hand, we concluded that we will have sufficient working capital on-hand to fund operations for at least 12 months from the date the unaudited condensed financial statements are issued. However, the perception that we may not be able to continue as a going concern may cause others to choose not to deal with us due to concerns about our ability to meet our contractual obligations.

Our ability to continue as a going concern requires that we obtain sufficient funding to finance our operations. If we are unable to obtain sufficient funding, our business, prospects, financial condition and results of operations will be materially and adversely affected and we may be unable to continue as a going concern. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide additional funding to us on commercially reasonable terms or at all.

Risks Related to the Development of AV-101

Our business is entirely dependent on the successful development, regulatory approval and commercialization of AV-101, our only product candidate under development.

We have invested substantially all of our efforts and financial resources in the development of AV-101 for the treatment of PAH, which has not been approved for sale or commercial use. Currently, AV-101 is our only product candidate and we have not licensed, acquired, or invented any other product candidates for preclinical or clinical evaluation. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a failure of a lead candidate. The success of our business, including our ability to finance our company and generate any revenue in the future, will, at this point, depend entirely on the successful development, regulatory approval and commercialization of AV-101, which may never occur. We may have inadequate financial or other resources to advance AV-101 through the clinical trial process, depending on the requirements of the FDA and similar foreign regulatory agencies. In addition, our clinical development program for AV-101 may not lead to regulatory approval from the FDA and similar foreign regulatory agencies if we fail to demonstrate that AV-101 is safe and effective in our planned Phase 2b/3 clinical trial, and we may therefore fail to commercialize AV-101. Further, AV-101 may not receive regulatory approval even if it is successful in planned and future clinical trials. Any failure to obtain regulatory approval of AV-101 would have a material and adverse impact on our business. Even if we successfully obtain regulatory approvals to market AV-101, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval. If the markets or patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of AV-101, even if approved.

We plan to seek regulatory approval to commercialize AV-101 in the United States and in selected foreign countries. The clinical and commercial success of AV-101 will depend on a number of factors, including the following:

- our ability to raise any additional required capital on acceptable terms, or at all;
- timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- whether we are required by the FDA or similar foreign regulatory agencies to conduct additional clinical trials or other studies beyond those planned to support approval of AV-101;
- our ability to consistently manufacture AV-101 on a timely basis;
- our ability, and the ability of any third parties with whom we contract, to remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with current Good Manufacturing Practices, or current GMPs;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, efficacy and acceptable risk-benefit profile of AV-101;

- the prevalence, duration and severity of potential side effects or other safety issues experienced with AV-101;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;
- achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to AV-101;
- the differentiation of AV-101 from other available approved, or investigational, drugs and treatments of PAH, and the willingness of physicians, operators of hospitals and clinics and patients to adopt and utilize AV-101 administered using a dry powder inhaler, or DPI;
- our ability to successfully develop a commercial strategy and thereafter commercialize AV-101 in the United States and internationally, if approved for marketing, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid and similar foreign authorities) and other third-party payors for AV-101;
- patients' willingness to pay out-of-pocket for AV-101 in the absence of coverage and/or adequate reimbursement from third-party payor;
- the convenience of the administration of AV-101 using our DPI;
- acceptance by physicians, payors and patients of the benefits, safety and efficacy of AV-101, if approved;
- patient demand for AV-101, if approved;
- our ability to establish and enforce intellectual property rights in and to AV-101; and
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize AV-101. Even if regulatory approvals are obtained, we may never be able to successfully commercialize AV-101. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of AV-101 to continue our business or achieve profitability.

While the scope of regulatory approval generally is similar in other countries, in order to obtain separate regulatory approval in other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy. For example, European regulatory authorities generally require a trial comparing the efficacy of the new drug to an existing drug prior to granting approval. Other countries also have their own regulations governing, among other things, clinical trials and commercial sales, as well as pricing and distribution of AV-101, and we may be required to expend significant resources to obtain regulatory approval and to comply with ongoing regulations in these jurisdictions. 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 have a negative effect on the regulatory process in others.

The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of AV-101. As a result of medical complications associated with PAH, the patient populations that AV-101 targets may be particularly susceptible to COVID-19, which may make it more difficult for us to identify patients able to enroll in our current and future clinical trials and may impact the ability of enrolled patients to complete any such trials.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. In December 2019, a novel strain of a virus named SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), or coronavirus, which causes COVID-19 spread to most countries across the world, including all 50 states within the United States. The COVID-19 pandemic is evolving, and has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. The extent to which the coronavirus impacts our operations or those of our third party partners,

including our preclinical studies or clinical trial operations, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak, new information that will emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others. The continued spread of COVID-19 globally, including the identification of new variants of COVID-19, could adversely impact our clinical trial operations, 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. Similar to other biopharmaceutical companies, we may experience protocol deviations or delays in initiating or completing our planned Phase 2b/3 clinical trial of AV-101, enrolling our clinical trial, or dosing of patients in our clinical trial as well as activating new trial sites. For example, we experienced a short delay in our Phase 1 trial when the study site shut down due to COVID-19. COVID-19 may also affect the third-party manufacturers of AV-101 and the DPI we plan to use in our Phase 2b/3 clinical trial, which could impact our ability to procure sufficient supplies and cause delays in our trial.

In addition, as a result of medical complications associated with PAH, the patient populations that AV-101 targets may be particularly susceptible to COVID-19, which may make it more difficult for us to identify patients able to enroll in our current and future clinical trials and may impact the ability of enrolled patients to complete any such trials. Any negative impact COVID-19 has to patient enrollment or treatment or the execution of our AV-101 clinical trials could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize AV-101, increase our operating expenses, and have a material adverse effect on our financial results. Timely enrollment in planned clinical trials is dependent upon clinical trial sites which could be adversely affected by global health matters, such as pandemics. We plan to conduct our Phase 2b/3 clinical trial for AV-101 in geographies which are currently affected by the COVID-19 pandemic. Some factors from the COVID-19 pandemic that will delay or otherwise adversely affect enrollment in the clinical trials of AV-101, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;
- limitations on travel that could interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face-to-face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;
- the potential negative affect on the operations of our third-party manufacturers;
- interruption in global shipping affecting the transport of clinical trial materials, such as investigational drug product, our DPIs and other supplies used in our clinical trials;
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments;
- operations, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether; and
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines.

We may be required to develop and implement additional clinical trial policies and procedures designed to help protect subjects from the COVID-19 virus. For example, in March 2020, the FDA issued a guidance, which the FDA has continued to periodically revise, on conducting clinical trials during the pandemic, which describes a number of considerations for sponsors of clinical trials impacted by the pandemic.

We have taken temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring our employees to work remotely, suspending all non-essential travel worldwide for our employees and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business. We cannot presently predict the scope and severity of the planned and potential shutdowns or disruptions of businesses and government agencies, such as the SEC, or FDA.

These and other factors arising from COVID-19 could worsen in countries that are already afflicted with COVID-19, particularly as new variants of the virus continue to be identified, or could continue to spread to additional countries. Any of these factors, and other factors related to any such disruptions that are unforeseen, could have a material adverse effect on our business and our results of operations and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize AV-101.

We have only recently begun testing of AV-101, a dry powder formulation of imatinib for the treatment of PAH administered using a DPI, to assess its safety and tolerability. Although we believe that AV-101 has therapeutic potential for PAH based on oral imatinib's results in the Phase 3 IMPRES trial, we are utilizing a novel dry powder formulation which may not achieve better or similar levels of clinical activity or may have similar tolerability challenges as oral imatinib. The results of earlier studies and trials of oral imatinib in PAH patients and our Phase 1 clinical trial of AV-101 may not be predictive of future trial results for AV-101.

The results of our Phase 1 clinical trial, as well as clinical testing of oral imatinib in PAH patients by third-parties, may not be predictive of the results of our planned Phase 2b/3 clinical trial. In the second half of 2021, we plan to initiate our Phase 2b/3 trial of AV-101 with a target enrollment of 200 patients in the Phase 2b portion and expect to report topline data from the Phase 2b portion of the trial in the middle of 2023. Our belief that AV-101 has a potential therapeutic benefit for PAH patients is based in part on the Phase 3 IMPRES trial conducted by Novartis AG, or Novartis, which showed oral administration of imatinib, marketed as Gleevec for multiple cancers led to statistically significant improvements across both primary and secondary endpoints in PAH patients on top of PAH standard of care therapies. Despite the statistically significant improvements in 6MWD and hemodynamics, there was no difference between oral imatinib and placebo in time to clinical worsening (TTCW), a composite endpoint consisting of death, hospitalization due to worsening PAH, worsening functional class, and a 15% reduction in 6MWD. However, oral imatinib was associated with significant adverse events that precluded its development as a therapy for PAH. AV-101 is our proprietary inhaled dry powder formulation of imatinib that delivers the medicine directly to the lung tissues using a DPI. While we have completed a Phase 1 clinical trial in 82 healthy volunteers, in which AV-101 demonstrated lower plasma levels of imatinib compared to 400 mg of oral imatinib and a favorable tolerability profile at a dose of up to 90 mg twice a day, AV-101 has not yet been tested in any patients with PAH to assess its efficacy and AV-101 may not have the same clinical activity as oral imatinib seen in the IMPRES trial. We also cannot be certain that AV-101 will continue to show similar tolerability when dosed in PAH patients as it did in healthy volunteers, and we may not be able to demonstrate to the satisfaction of the FDA the safety, efficacy and acceptable risk-benefit profile of AV-101 during our planned Phase 2b/3 clinical trial. As a result, even if AV-101 does achieve lower imatinib plasma concentrations in our Phase 2b/3 clinical trial, there can be no assurance that AV-101 will exhibit similar tolerability as compared to our Phase 1 trial or improved tolerability as compared to the IMPRES trial of oral imatinib. Product candidates in later stages of clinical trials may fail to show the desired pharmacological properties or safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the pharmaceutical and biotechnology industries, including Novartis in the IMPRES trial of oral imatinib, have suffered significant setbacks in Phase 3 clinical trials, even after positive results in earlier clinical trials. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. Notwithstanding any promising results in our Phase 1 clinical trial, we cannot be certain that we will not face similar setbacks.

Additionally, we may utilize "open-label" trial designs or open-label extensions to our clinical trials in the future. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic

effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial or extension may not be predictive of future clinical trial results with AV-101 when studied in a controlled environment with a placebo or active control.

As a result of the foregoing, even if we are able to complete any planed and future clinical trials of AV-101, the results may not be sufficient to obtain regulatory approval.

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

The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. We plan to initiate our Phase 2b/3 clinical trial of AV-101 in the second half of 2021. The Phase 2b portion of this trial will be a dose-ranging trial in which PVR will be the primary endpoint and will have a target enrollment of 200 patients. The Phase 3 portion of the trial will be based on the optimal dose selected in the Phase 2b portion with 6MWD as the primary endpoint. The enrollment of patients depends on many additional factors, including:

- size and nature of the patient population and process for identifying patients;
- the severity of the disease under investigation;
- the availability and efficacy of approved drugs for the disease under investigation;
- the patient eligibility criteria defined in the protocol;
- the impact of COVID-19 on our ability to identify patients able to enroll in our clinical trials and the ability of enrolled patients to complete our clinical trials;
- the general willingness of patients to enroll in the trial;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience, and to obtain Investigational Review Board, or IRB, approval to conduct our trial at U.S. sites, and similar approvals at sites outside the U.S.;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new therapies that may be approved for the indications we are investigating;
- competition for patients from other investigational clinical trials in PAH being conducted at the same time as our Phase 2b/3 trial;
- the clinical site's ability to obtain and maintain patient consents;
- delays in or temporary suspension of the enrollment of patients in our planned clinical trial due to the COVID-19 pandemic; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion, including as a result of contracting COVID-19 or other health conditions or being forced to quarantine.

Enrollment risks are heightened with respect to indications that are rare or orphan diseases, which may limit the pool of patients that may be enrolled in our planned clinical trials. We are developing AV-101 for the treatment of PAH, which is an orphan disease and does not have a large patient population. As a result, we may encounter difficulties enrolling subjects in our clinical trials evaluating AV-101 for the treatment of PAH due, in part, to the small size of this patient population.

In addition, our clinical trials may compete with other clinical trials for product candidates that seek to treat PAH, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we may conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of AV-101.

Clinical development involves a lengthy and expensive process with an uncertain outcome, and delays can occur for a variety of reasons outside of our control.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. We have completed our Phase 1 trial of AV-101 in healthy volunteers and expect to commence our Phase 2b/3 dose-ranging clinical trial in PAH patients in the second half of 2021. The FDA has agreed in principle with the proposed study design of our Phase 2b/3 efficacy trial, dose strengths, statistical analysis and that a single efficacy study with strong results could be sufficient to support a 505(b)(2) NDA. However, changes in regulatory requirements and guidance may occur and we may need to amend our clinical trial protocol to reflect these changes with appropriate regulatory authorities. In addition, we may experience delays in initiating or completing our planned studies and trials of AV-101. Furthermore, we cannot be certain that studies or trials for AV-101 will begin on time, not require redesign, enroll an adequate number of subjects on time or be completed on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delays or failures related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical trials;
- delays in obtaining regulatory authorization to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining institutional review board, or IRB, approval at each trial site;
- recruiting an adequate number of suitable patients to participate in a trial;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- having subjects complete a trial or return for post-treatment follow-up;
- clinical sites deviating from trial protocol or dropping out of a trial;
- addressing subject safety concerns that arise during the course of a trial;
- adding a sufficient number of clinical trial sites; or
- obtaining sufficient quantities of AV-101 for use in clinical trials from third-party suppliers on a timely basis.

We may experience numerous adverse or unforeseen events during, or as a result of, preclinical studies and clinical trials that could delay or prevent our ability to receive marketing approval or commercialize AV-101, including:

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of AV-101 may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon our development program for AV-101;
- the number of patients required for clinical trials of AV-101 may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;

- we or our third-party contractors may fail to comply with regulatory requirements, fail to maintain adequate quality controls, or be unable to produce sufficient product supply to conduct and complete clinical trials of AV-101 in a timely manner, or at all;
- we or our investigators might have to suspend or terminate clinical trials of AV-101 for various reasons, including non-compliance with regulatory requirements, a finding that AV-101 has undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of AV-101 may be greater than we anticipate;
- the quality of our active pharmaceutical ingredient or other materials necessary to conduct clinical trials of AV-101 may be insufficient or inadequate;
- the FDA may determine that we cannot rely on the Section 505(b)(2) approval pathway for AV-101, in which case we may be required to conduct additional clinical trials and provide additional data and information and meet additional standards for product approval;
- the FDA may determine that we have identified the wrong listed drug(s), or LD, or that approval of a Section 505(b)(2) application for AV-101 is blocked by patent or non-patent exclusivity of the LD or LDs;
- regulators may revise the requirements for approving AV-101, or such requirements may not be as we anticipate; and
- future collaborators may conduct clinical trials in ways they view as advantageous to them but that are sub-optimal for us.

If we are required to conduct additional clinical trials or other testing of AV-101 beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of AV-101 or other testing, if the results of these trials or tests are not positive or are only moderately positive or if there are safety concerns, we may:

- incur unplanned costs;
- be delayed in obtaining marketing approval for AV-101 or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements, which could be expensive and time consuming; or
- have the treatment removed from the market after obtaining marketing approval.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or ethics committees of the institutions in which such trials are being conducted, by the Data Safety Monitoring Board, if any, for such clinical trial or by the FDA or other regulatory authorities. Such authorities may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Further, we plan to conduct our Phase 2b/3 clinical trial for AV-101 in PAH patients globally. This presents additional risks that may delay completion of our clinical trial. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and

any related compensation result in perceived or actual conflicts of interest, or a regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing AV-101.

If any of our clinical trials of AV-101 are unsuccessful, delayed or terminated, its commercial prospects may be harmed, and our ability to generate revenues from sales of AV-101 will be delayed or not realized at all. In addition, any delays in completing our clinical trials may increase our costs, slow down our AV-101 development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of AV-101. If AV-101 generally proves to be ineffective, unsafe or commercially unviable, it would have a material and adverse effect on our business, financial condition, results of operations and prospects.

AV-101 may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

The results of our preclinical studies or clinical trials may show that AV-101 may cause undesirable side effects, which could interrupt, delay or halt clinical trials, resulting in the denial of regulatory approval by the FDA and other regulatory authorities. In light of widely publicized events concerning the safety risk of certain drug products, regulatory authorities, members of Congress, the Government Accounting Office, medical professionals and the general public have raised concerns about potential drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling or boxed warnings that further limit use of the drug products and establishment of risk management programs that may, for instance, restrict distribution of drug products. The increased attention to drug safety issues may result in a more cautious approach by the FDA to clinical trials. Data from clinical trials may receive greater scrutiny with respect to safety, which may make the FDA or other regulatory authorities more likely to terminate clinical trials before completion, or require longer or additional clinical trials that may result in substantial additional expense and a delay or failure in obtaining approval or approval for a more limited indication than originally sought.

While AV-101 was generally well-tolerated in our Phase 1 clinical trial, subjects treated with 90 mg of AV-101, the highest dose in this trial, reported a higher frequency of adverse events, including cough at the time of inhalation of the dry powder and headache. However, all adverse events were generally mild and transient, and no patients discontinued the study due to these adverse events. The only adverse events experienced by subjects treated at lower doses of AV-101 in the Phase 1 MAD portion of the trial were cough at dosing (1 of 9 patients in the medium dose and 1 of 9 patients at the low dose) and throat irritation (1 patient of 9 at the medium dose). In contrast, the Phase 3 IMPRES trial of oral imatinib in PAH patients demonstrated significant AEs, including nausea, edema, vomiting and diarrhea. Despite the clinical effects of oral imatinib on their disease, 26% of patients on oral imatinib and 7% of placebo patients discontinued due to AEs by 24 weeks of the trial. Further development of oral imatinib for the treatment of PAH was discontinued by Novartis. We believe that delivery of imatinib directly to the lungs through our proprietary dry powder formulation has the potential to maximize the amount of drug in the targeted tissues while minimizing systemic exposure and minimizing the potential for serious adverse events. Nevertheless, if unacceptable side effects arise in our Phase 2b/3 clinical trial or other trials we may conduct, we, the FDA, or the IRBs at the institutions in which our studies are conducted could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of AV-101 for PAH.

If AV-101 receives marketing approval and we or others later identify undesirable side effects caused by such product or by other imatinib products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approvals of the product, or seek an injunction against its manufacture or distribution;
- we may be required to recall a product or change the way such product is administered to patients or conduct additional clinical trials or post-approval studies;

- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be required to add additional warnings or boxed warnings to our drug labeling or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we may be required to implement a Risk Evaluation and Mitigation Strategy, or REMS, which may include distribution or use restrictions;
- we could be sued and held liable for harm caused to patients;
- we may be subject to fines, injunctions or the imposition of criminal penalties;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business.

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

From time to time, we may publicly disclose preliminary, interim or topline data from our preclinical studies and clinical trials. These interim updates are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies or trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. 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. Adverse changes between interim data and final data could significantly harm our business and prospects. Further, additional disclosure of interim data by us or by our competitors in the future could result in volatility in the price of our common stock.

In addition, the information we choose to publicly disclose regarding a particular study or trial is typically selected from a more extensive amount of available information. Investors may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the preliminary or topline data that we report differ from late, final or actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, any of our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

We intend to use the 505(b)(2) regulatory pathway to seek regulatory approval of AV-101, but if the FDA concludes that our marketing application no longer qualifies for the Section 505(b)(2) regulatory pathway, then our application may not be accepted by the FDA for review and approval may be delayed.

We intend to seek FDA approval for AV-101 for PAH through the Section 505(b)(2) regulatory pathway. Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, or FDCA, was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, and permits the submission of an NDA where at least some of the information required for approval comes from preclinical studies or clinical trials not conducted by or for the applicant and for which the applicant has not obtained

a right of reference. The FDA interprets Section 505(b)(2) of the FDCA to permit the applicant to rely upon the FDA's previous findings of safety and efficacy for an approved product. The FDA requires submission of information needed to support any changes to a previously approved drug, such as published data or new studies conducted by the applicant or clinical trials demonstrating safety and efficacy. The FDA could require additional information to sufficiently demonstrate safety and efficacy to support approval. If the FDA later determines AV-101 does not meet the requirements of Section 505(b)(2), or that additional information is needed to support a marketing application for AV-101, we could experience delays in submitting a marketing application or in obtaining marketing approval. Moreover, even if AV-101 is approved under the Section 505(b)(2) regulatory pathway, the approval may be subject to limitations on the indicated uses for which it may be marketed or to other conditions of approval, or may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the products.

Risks Related to Commercialization

We face, and will continue to face, significant competition and our failure to effectively compete may prevent us from achieving significant market penetration for AV-101, if approved. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete.

The pharmaceutical industry is highly competitive, with a number of established, large pharmaceutical companies, as well as many smaller companies. Many of these companies have greater financial resources, marketing capabilities and experience in obtaining regulatory approvals for product candidates. There are several pharmaceutical companies, biotechnology companies, public and private universities, government agencies and research organizations actively engaged in research and development of products to target PAH. We expect AV-101 to compete on the basis of, among other things, efficacy, safety, convenience, price, and the availability of reimbursement from commercial, government and other third-party payors. One or more of our competitors may develop products based upon the principles underlying our proprietary technologies earlier than us, obtain approvals for such products from the FDA more rapidly than us or develop alternative products or therapies that are safer, more effective and/or more cost effective than AV-101. We also expect to face competition in our efforts to identify appropriate collaborators or partners to help commercialize AV-101 in our target commercial areas.

If approved, AV-101 is expected to face competition from drug products that are already on the market, as well as those in clinical development. In particular, we expect that AV-101 will face competition from prostanoids available in oral form as Orenitram (United Therapeutics Corporation, or United Therapeutics) and Uptravi (Janssen Pharmaceuticals, Inc., or Janssen), by inhalation as Tyvaso (United Therapeutics), and by infusion as Remodulin (United Therapeutics), which are existing drug products indicated for the treatment of PAH, potential new entrants such as sotatercept (Acceleron Pharma, Inc.), and/or, seralutinib (Gossamer Bio, Inc.), as well as generic equivalents of Tyvaso following the expiry of Tyvaso's patent in 2018. On October 15, 2018, United Therapeutics Corporation, or United Therapeutics, and MannKind closed their worldwide exclusive licensing and collaboration agreement for the development and commercialization of a dry powder formulation of treprostinil, an investigational product currently being evaluated in clinical trials for the treatment of PAH. Under the agreement, United Therapeutics will be responsible for global development, regulatory and commercial activities. MannKind will manufacture clinical supplies and initial commercial supplies of the product while long-term commercial supplies will be manufactured by United Therapeutics. United Therapeutics announced that they filed an NDA for the inhaled dry powder formulation of treprostinil in April. Additionally, we are aware that Arena Pharmaceuticals, Inc., or Arena, has commenced a Phase 3 trial evaluating ralinepag, an oral prostanoid product for the treatment of patients suffering from PAH. On January 24, 2019, Arena and United Therapeutics closed on a global license agreement for ralinepag. Under the agreement, United Therapeutics is now responsible for the development, manufacture and commercialization of ralinepag. These collaborations may accelerate competition for AV-101. We believe that AV-101, if approved, could be used prior to or in combination with prostanoids, and in combination with existing front-line agents such as the oral PDE5 inhibitors, including Revatio (Pfizer Inc.) and Adcirca (United Therapeutics); the sGC stimulator Adempas (Bayer AG); and oral ERAs, including Tracleer (Janssen), Letairis (Gilead Sciences, Inc.) and Opsumit (Janssen). PAH is also an active indication for investigational drugs, and we may face competition in the future from sotatercept (Acceleron Pharma, Inc.), and/or, seralutinib (Gossamer Bio, Inc.). To our knowledge, Tenax Therapeutics, Inc. and Aerami Therapeutics, Inc. have communicated interest in developing imatinib for PAH, and both companies are at a preclinical stage of development.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources and experience than we do. If we successfully obtain approval for AV-101, we will face competition based on many different factors, including the safety and effectiveness of AV-101, the ease with which AV-101 can be administered and the extent to which patients accept the nasal route of administration, the timing and scope of regulatory approvals for AV-101, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, by being more effective, safer, less expensive or marketed and sold more effectively than AV-101. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing AV-101. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. For additional information regarding our competition, see the section titled "Business—Competition".

If the FDA or comparable regulatory authorities approve generic versions of AV-101, or do not grant AV-101 a sufficient period of market exclusivity before approving its generic version, our ability to generate revenue may be adversely affected.

Once a NDA is approved, including under the 505(b)(2) pathway, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials to assess safety and efficacy. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labelling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug is typically lost to the generic product.

Generic drug manufacturers may seek to launch generic products following the expiration of any applicable exclusivity period we obtain if AV-101 is approved, even if we still have patent protection. Competition that AV-101 could face from generic versions could materially and adversely affect our future revenue, profitability, and cash flows and substantially limit our ability to obtain a return on the investments we have made in AV-101.

If the market opportunity for AV-101 is smaller than we estimate or if any regulatory approval that we obtain is based on a narrower definition of the patient population, our revenue and ability to achieve profitability will be adversely affected, possibly materially.

The incidence and prevalence for target patient populations of AV-101 has not been established with precision. AV-101 is an inhaled dry powder formulation of anti-proliferative imatinib for people who suffer from PAH. A DPI is used to deliver the medicine directly to lung tissues, enabling treatment of the diseased tissues directly while reducing the amount of drug delivered to other organs in the body which can cause unwanted adverse events. Our projections of both the number of people who have PAH, as well as the subset of people with PAH who have the potential to benefit from AV-101, are based on our estimates.

The total addressable market opportunity will ultimately depend upon, among other things, the patient criteria included in the final label, the indications for which AV-101 is approved for sale, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients with PAH for which AV-101 may be approved as treatment may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our products, or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. AV-101 is our only product candidate and therefore our business is dependent on the market opportunity for our product.

The successful commercialization of AV-101 will depend in part on the extent to which governmental authorities, private health insurers, and other third-party payors provide coverage and adequate reimbursement levels. Failure to obtain or maintain coverage and adequate reimbursement for AV-101, if approved, could limit our ability to market our product and decrease our ability to generate revenue.

In the United States and markets in other countries, patients generally rely on third-party payors to be able to afford medical services and pharmaceutical products that receive FDA approval. Our ability to successfully

commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. A decision by a third-party payor not to cover or separately reimburse for AV-101, could reduce physician utilization if approved. Assuming there is coverage for AV-101 by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the United States, the European Union, or EU, or elsewhere will be available for AV-101 and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. Private third-party payors tend to follow Medicare coverage policies and payment limitations in setting their own reimbursement rates to a substantial degree, but also have their own methods and approval process apart from Medicare determinations. As a result, the coverage determination process is often a time-consuming and costly process that may require us to provide scientific and clinical support for the use of AV-101 to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely. Factors payors consider in determining reimbursement are based on whether the product is: (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational.

Moreover, increasing efforts by governmental and other third-party payors in the United States and abroad to cap or reduce healthcare costs have resulted in increasing challenges to prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and adequate reimbursement for particular drugs when an equivalent generic drug, biosimilar or a less expensive therapy is available. Even if we show improved efficacy or improved convenience of administration with AV-101, pricing of existing third-party therapeutics may limit the amount we will be able to charge for it. These third-party payors may deny or revoke the reimbursement status of AV-101, if approved, or establish prices for it at levels that are too low to enable us to realize an appropriate return on our investment. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize AV-101.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

Outside the United States, pharmaceutical products are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries will likely put pressure on the pricing and usage of medical products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for AV-101. Accordingly, in markets outside the United States, the reimbursement for AV-101 may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits.

Even if AV-101 obtains regulatory approval, it may fail to achieve market acceptance.

Even if AV-101 receives FDA or other regulatory approvals, its commercial success will depend significantly on its adoption and use by physicians and patients for approved indications. The degree of market acceptance of AV-101, if approved, will depend on a number of factors, including:

- the safety and efficacy of AV-101 as compared to other available treatments for PAH;
- patient satisfaction with the results and administration of AV-101 and overall treatment experience, including, the ease and convenience of administration of AV-101;
- the perceived advantages of AV-101 over alternative treatments, such as prostacylins;
- the clinical indications for which AV-101 is approved and patient demand for approved products that treat those indications;
- our ability to manufacture and release adequate commercial supplies on a timely basis;
- the availability of coverage and adequate reimbursement from managed care plans, private insurers, government payors (such as Medicare and Medicaid) and other third-party payors for AV-101;
- the cost of treatment with AV-101 in relation to alternative treatments and patients' willingness to pay out-of-pocket for the product, if approved, in the absence of coverage and/or adequate reimbursement from third-party payors;
- acceptance by physicians, operators of hospitals and clinics and patients of the product as a safe, effective and easy to administer treatment;
- physician and patient willingness to adopt a new therapy over other available preventive and acute therapies for treatment of PAH;
- the prevalence and severity of side effects;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about AV-101 or favorable publicity about competitive products;
- patients' willingness to take a dry-powder inhaled medication;
- potential product liability claims; and
- the approval of other new therapies for the same indication.

We cannot assure you that AV-101, if approved, will achieve market acceptance among physicians and patients. Any failure by AV-101, if approved, to achieve market acceptance or commercial success would adversely affect our results of operations.

We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell AV-101 effectively in the United States and foreign jurisdictions, if approved, or generate product revenue.

We currently do not have a marketing or sales organization. In order to commercialize AV-101, if approved, in the United States and foreign jurisdictions, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If AV-101 receives regulatory approval, we expect to establish a sales organization in the United States with technical expertise and supporting marketing and distribution capabilities to commercialize it, which will be expensive and time consuming. As a company, Aerovate has no prior experience in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of AV-101. We may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize AV-101. If we are not successful in commercializing AV-101, either on our own or through arrangements with one or more third parties, we may not be able to generate product revenue and we would incur significant additional losses.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of AV-101.

We face an inherent risk of product liability as a result of the planned clinical testing of AV-101 and will face an even greater risk if we commercialize it. For example, we may be sued if AV-101 allegedly causes injury.

Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of AV-101. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for AV-101;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize AV-101.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of AV-101. We currently carry product liability insurance covering our clinical trials, however, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any dose of AV-101, we intend to expand our insurance coverage to include its sale; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all.

Risks Related to Our Reliance on Third Parties

We rely, and intend to continue to rely, on qualified third parties to supply all components of AV-101. As a result, we are dependent on several third parties, some of which are sole source suppliers, for the manufacture of AV-101 and our supply chain, and if we experience problems with any of these suppliers, or they fail to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, it would materially and adversely affect our business.

We do not own or operate manufacturing facilities for clinical or commercial manufacture of either our proprietary dry-powder formulation of imatinib or the DPI, including the drug substance and packaging. We have limited personnel with experience in drug-device product manufacturing and we lack the capabilities to manufacture either the drug component of AV-101 or the DPI on a clinical or commercial scale. We outsource all manufacturing and packaging of AV-101 to third parties and obtain the DPI from a sole source supplier, and we do not plan to own or operate our own manufacturing and packaging facilities. There can be no assurance that our clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. For example, three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and more are likely to be authorized in the coming months. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, has placed strain on manufacturing supply chains and may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. In particular, any replacement of any of our third-party suppliers could require significant effort and expertise because there may be a limited number of qualified replacements.

Certain of our suppliers are subject to regulatory requirements covering manufacturing, testing, quality control and record keeping relating to AV-101, and are subject to pre-approval and ongoing inspections by the

regulatory agencies. Failure by any of our suppliers to comply with applicable regulations may result in long delays and interruptions to our manufacturing capacity while we seek to secure another supplier that meets all regulatory requirements.

Reliance on third-party manufacturers entails risks that we would more directly manage and control, or to which we would not be subject, if we manufactured AV-101 ourselves, including:

- reliance on the third parties for regulatory compliance, quality assurance and hazardous materials handling;
- the possible breach of the manufacturing and quality agreements by the third parties because of factors beyond our control;
- the possibility of termination or nonrenewal of the agreements by the third parties because of our breach of the manufacturing agreement or based on their own business priorities;
- with respect to any manufacturers with which we do not have a long-term agreement, the possibility that the manufacturer decides to stop supplying to us or changes the price or other terms of supply; and
- Changes in the products produced by our suppliers, such that they satisfy specifications but have an unanticipated negative impact on the performance of AV-101.

Any of these factors could cause the delay of required approvals or commercialization of AV-101, could prevent us from commercializing it successfully, could cause the suspension of initiation or completion of clinical trials and regulatory submissions, and could lead to higher product costs.

In addition, the facilities used by our contract manufacturing organizations, or CMOs to manufacture AV-101 are subject to various regulatory requirements and may be subject to inspection by the FDA or other regulatory authorities. We do not directly control manufacturing at our CMOs, and are completely dependent on them for compliance with current regulatory requirements. If our CMOs for AV-101 cannot successfully manufacture components of finished product that conforms to our specifications and the regulatory requirements of the FDA or comparable regulatory authorities in foreign jurisdictions, we may not be able to rely on them for the manufacture of AV-101. If we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce AV-101 according to the specifications previously submitted to the FDA or another regulatory authority. In addition, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. In addition, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds our facilities or those of our CMOs inadequate for the manufacture of AV-101 or if such facilities are subject to enforcement action in the future or are otherwise inadequate, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or commercialize AV-101 and the timing of any such approval and commercialization.

Additionally, our CMOs may experience manufacturing difficulties due to resource constraints or as a result of labor shortages, disputes or unstable political environments or on account of global pandemics or similar events, including the COVID-19 pandemic and its continued spread. If our CMOs were to encounter any of these difficulties, our ability to provide AV-101 to patients in clinical trials, or to provide product for the treatment of patients once approved, would be jeopardized.

We rely, and intend to continue to rely, on third parties in the conduct of all of our clinical trials. If these third parties do not successfully carry out their contractual duties, fail to comply with applicable regulatory requirements or meet expected deadlines, we may be unable to obtain regulatory approval for AV-101.

We currently do not have the ability to independently conduct any clinical trials. The FDA and comparable foreign regulatory authorities in other jurisdictions require us to comply with regulations and standards, commonly referred to as good clinical practice, or GCP, requirements for conducting, monitoring, recording and reporting the results of clinical trials, in order to ensure that the data and results are scientifically credible and accurate and that the trial subjects are adequately informed of the potential risks of participating in clinical trials. We rely on medical institutions, clinical investigators, contract laboratories and other third parties, such as CROs, to conduct GCP-compliant clinical trials of AV-101 properly and on time. Our global Phase 2b/3 clinical trial will be managed by one CRO and carried out in over 20 countries and numerous clinical sites. While we have agreements with these third parties, we monitor and control only certain aspects of their activities

and have limited influence over their actual performance and the amount or timing of resources that they devote to our programs. Third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. The third parties with whom we contract for execution of our clinical trials play a significant role in the conduct of these trials and the subsequent collection and analysis of data. Although we rely on these third parties to conduct our clinical trials, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations, and our reliance on these third parties does not relieve us of our regulatory responsibilities.

If the third parties conducting our clinical trials do not adequately perform their contractual duties or obligations, experience significant business challenges, disruptions or failures, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the data they obtain is compromised due to their failure to adhere to our protocols or to GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and clinical trials may need to be extended, delayed, terminated or repeated. As a result, we may not be able to obtain regulatory approval in a timely fashion, or at all, for AV-101, our results our business and results of operations and the commercial prospects for AV-101 would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We rely on third parties to supply the raw materials to produce AV-101.

We will rely on independent third parties to supply the raw materials that we use to produce AV-101. As such, we will be dependent upon their services and will not be in a position to control their operations as we might if we directly produced these raw materials. We do not have supplier contracts with these third parties. Although we believe the raw materials used to manufacture our products are readily available and can be obtained from multiple reliable sources on a timely basis, circumstances outside our control may impair our ability to have an adequate supply of raw materials to produce AV-101 which could lead to production delays, interruptions or the need to identify and qualify new raw materials in the production of AV-101.

We may seek to establish collaborations, and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

Our product development program and the potential commercialization of AV-101 will require substantial cash to fund expenses. We may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of AV-101.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's own evaluation of a potential collaboration. Such factors a potential collaborator will use to evaluate a collaboration may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for AV-101, the costs and complexities of manufacturing and delivering AV-101 to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for AV-101. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

We may also be restricted under collaboration agreements from entering into future agreements on certain terms with potential collaborators. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of AV-101 for which we are seeking to collaborate, reduce or delay its development program, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization

activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop AV-101 or bring it to market and generate product revenue.

In addition, any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

Risks Related to Our Intellectual Property

We have many pending patent applications with respect to AV-101, but do not own any issued patents. We can provide no assurance that any of our current or future patent applications will result in issued patents. If we cannot protect our patent rights or our other proprietary rights, others may develop products similar or identical to ours, and we may not be able to compete effectively in our market or successfully commercialize any product candidates we may develop.

Our success depends to a significant degree upon whether we can continue to secure, enforce and defend intellectual property rights that protect our AV-101 product candidate and to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of others. If we are unable to obtain and maintain sufficient intellectual property protection for AV-101 or other product candidates that we may identify, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors and other third parties could develop and commercialize product candidates similar or identical to ours, and our ability to successfully commercialize AV-101 and other product candidates that we may pursue may be impaired. We do not own any issued patents with respect to AV-101, and we can provide no assurance that any of our current or future patent applications will result in issued patents or that any issued patents will provide us with any competitive advantage. Failure to obtain such issued patents could have a material adverse effect on our ability to develop and commercialize our product candidates. Furthermore, other parties may successfully challenge, invalidate or circumvent our issued patents so that our patent rights do not create an effective competitive barrier or revenue source.

We seek to protect our proprietary position by, among other things, filing patent applications in the United States and abroad related to our proprietary technologies, development programs and product candidates. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications or to maintain, defend and enforce any patents that may issue from such 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 currently own a number of U.S. provisional patent applications. U.S. provisional patent applications are not eligible to become issued patents until, among other things, we file a non-provisional patent application within 12 months of filing of one or more of our related provisional patent applications. With regard to such U.S. provisional patent applications, if we do not timely file any non-provisional patent applications, we may lose our priority date with respect to our provisional patent applications and any patent protection on the inventions disclosed in our provisional patent applications. Further, in the event that we do timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patents or if such issued patents will provide us with any competitive advantage.

Further, any of our provisional or non-provisional patent applications may fail to result in issued patents with claims that cover our proprietary products and technology, including our AV-101 product candidate or any other product candidate in the United States or in other foreign countries, in whole or in part. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third

parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal, technological and factual questions and has, in recent years, been the subject of much debate and litigation throughout the world. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. The subject matter claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Therefore, our pending and future patent applications may not result in patents being issued in relevant jurisdictions that protect our product candidates, in whole or in part, or which effectively prevent others from commercializing competitive product candidates, and even if our patent applications issue as patents in relevant jurisdictions, they may not issue in a form that will provide us with any meaningful protection for our product candidates or technology, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Additionally, our competitors may be able to circumvent our patents by developing similar or alternative product candidates or technologies in a non-infringing manner.

In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Without patent protection for our current or future product candidates, we may be open to competition from generic versions of such products. 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 patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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. We may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or the USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others, or other proceedings in the USPTO or applicable foreign offices that challenge priority of invention or other features of patentability. An adverse determination in any such submission, proceeding or litigation could result in loss of exclusivity or freedom to operate, patent claims being narrowed, invalidated or held unenforceable, in whole or in part, limit the scope or duration of the patent protection of AV-101, all of which could limit our ability to stop others from using or commercializing similar or identical product candidates or technology to compete directly with us, without payment to us, or result in our inability to manufacture or commercialize product candidates or approved products (if any) without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates, or could have a material adverse effect on our ability to raise funds necessary to continue our research programs or clinical trials. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us.

We cannot be certain that the USPTO and courts in the United States or the patent offices and courts in foreign countries will consider the claims in our patents and applications covering our AV-101 product candidate and possible future product candidates as patentable. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products off-label. Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent, including through legal action.

If we lose or cannot obtain patent protection for our AV-101 product candidate or other future product candidates it could have a material adverse impact on our business.

Intellectual property litigation could cause us to spend substantial resources and prevent us from pursuing our programs.

From time to time we may have to defend our intellectual property rights. If we are involved in an intellectual property dispute, we may need to litigate to defend our rights or assert them against others. Disputes can

involve arbitration, litigation or proceedings declared by the USPTO or the International Trade Commission or foreign patent authorities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to 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.

If we were to initiate legal proceedings against a third party to enforce a patent covering our product candidate, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the United States and in Europe, 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, for example, lack of novelty, obviousness or non-enablement. Third parties might allege unenforceability of our patents because during prosecution of the patent an individual connected with such prosecution withheld relevant information or made a misleading statement. The outcome of proceedings involving assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity of patents, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution, but that an adverse third party may identify and submit in support of such assertions of invalidity. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidate. Our patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Third parties may initiate or threaten legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our strategic partners to develop, manufacture, market and sell our drugs and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. Extensive litigation regarding patents and other intellectual property rights is common in the biotechnology and pharmaceutical industries. We may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our drugs and technology, including interference, derivation, reexamination, post-grant review, opposition, cancellation or similar proceedings before the USPTO or its foreign counterparts. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, resulting in payment of damages. These damages potentially include increased damages and attorneys' fees if we are found to have infringed such rights willfully. Parties making claims against us may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. We may not be aware of all such intellectual property rights potentially relating to our drugs and their uses. If a third party claims that our AV-101 product candidate or our technology infringe its patents or other intellectual property rights, we or our partners may have to discontinue an important product or product line, alter our products and processes, pay license fees or cease certain activities. We could be required to obtain a license from such third party in order to continue developing and commercializing AV-101 or other product candidates. However, we may not be able to obtain a license to needed intellectual property on commercially reasonable terms, if at all. Even if a license can be obtained on reasonable terms, the rights may be nonexclusive, which would give our competitors access to the same intellectual property

rights. We might also be forced to redesign or modify our product candidates so that we no longer infringe the third-party intellectual property rights, which may result in significant cost or delay to us, or which redesign or modification could be impossible or technically infeasible. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or patent applications held by others that relate to our business. This is especially true since patent applications in the United States are filed confidentially for the first 18 months. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain. Thus, we do not know with certainty that our drugs or our intended commercialization thereof, does and will not infringe or otherwise violate any third party's intellectual property.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on drugs in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those we could obtain in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products. In addition, competitors may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patent rights or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop competitors from infringing our patent rights or misappropriating our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit our right to enforce our patent rights against third parties, including government agencies, government contractors, or doctors. In these countries, patents may provide limited or no benefit. We must ultimately seek patent protection on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

In addition, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patent rights 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 rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent protection for AV-101, our business may be materially harmed.

Depending upon the timing, duration and specifics of the first FDA marketing authorization of AV-101, a United States patent that we own may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments allow the owner of an approved product to extend patent protection for up to five years as compensation for patent term lost during product development and the FDA regulatory review process. During this period of extension, the scope of protection is limited to the approved product and approved uses.

Although we plan on seeking patent term restoration for our products, we may not succeed if, for example, we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we cannot obtain patent term restoration or the term of any such patent restoration is less than we request, our competitors may enter the market and compete against us sooner than we anticipate, and our ability to generate revenue could be materially adversely affected.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent which might adversely affect our ability to develop, manufacture and market our product candidate.

We cannot guarantee that any of our patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States, Europe and elsewhere that is relevant to or necessary for the commercialization of AV-101 in any jurisdiction. For example, in the United States, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States, EU and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our product candidates could be filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover AV-101 or the use of AV-101. After issuance, the scope of patent claims remains subject to construction as determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our product candidates. We may incorrectly determine that AV-101 is not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States, the EU or elsewhere that we consider relevant may be incorrect, which may negatively impact our ability to develop and market AV-101. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market AV-101.

If we fail to correctly identify or interpret relevant patents, we may be subject to infringement claims. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we fail in any such dispute, in addition to being forced to pay monetary damages, we may be temporarily or permanently prohibited from commercializing AV-101. We might, if possible, also be forced to redesign AV-101 in a manner that no longer infringes third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Changes in United States patent law could diminish the value of patents in general, thereby impairing our ability to protect AV-101.

Recent court rulings, including rules from the United States Supreme Court, have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

In addition, the America Invents Act, or the AIA, which was passed in September 2011, resulted in significant changes to the U.S. patent system. An important change introduced by the AIA is that, as of March 16, 2013, the United States transitioned from a "first-to-invent" to a "first-to-file" system for deciding which party should be granted a patent when two or more patent applications are filed by different parties claiming the same invention. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. A third party that files a patent application in the USPTO after that date but before us could therefore be awarded a patent covering an invention of ours even if we made the invention before it was made by the third party. This will require us to be cognizant going forward

of the time from invention to filing of a patent application and diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions.

Among some of the other changes introduced by the AIA are changes that limit where a patentee may file a patent infringement suit and providing opportunities for third parties to challenge any issued patent in the USPTO. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action.

Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. It is not clear what, if any, impact the AIA will have on the operation of our business. However, the AIA 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.

We may become involved in opposition, interference, derivation, inter partes review or other proceedings challenging our patent rights, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

There may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns.

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

The USPTO and European and other 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 and annuity fees on any issued patent are due to be paid to the USPTO and European and other patent agencies over the lifetime of a patent. While an inadvertent failure to make payment of such fees or to comply with such provisions can in many cases be cured by additional payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance with such provisions will result in the abandonment or lapse of the patent or patent application, and the partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents within prescribed time limits. If we fail to maintain the patents and patent applications covering AV-101 or if we otherwise allow our patents or patent applications to be abandoned or lapse, it can create opportunities for competitors to enter the market, which would hurt our competitive position and could impair our ability to successfully commercialize our product candidates in any indication for which they are approved.

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

We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own. The issuance of a patent is not conclusive as to its inventorship.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We could in the future be subject to claims that we or our employees have inadvertently or otherwise used or disclosed alleged trade secrets or other confidential information of former employers or competitors. Although we try to ensure that our employees and consultants do not use the intellectual property, proprietary information, know-how or trade secrets of others in their work for us, we may become subject to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement, or that we or these individuals have, inadvertently or otherwise, used or disclosed the alleged trade secrets or other proprietary information of a former employer or competitor.

While we may litigate to defend ourselves against these claims, even if we are successful, litigation could result in substantial costs and could be a distraction to management. If our defenses to these claims fail, in addition to requiring us to pay monetary damages, a court could prohibit us from using technologies or features that are essential to our product candidates, if such technologies or features are found to incorporate or be derived from the trade secrets or other proprietary information of the former employers. Moreover, any such litigation or the threat thereof may adversely affect our reputation, our ability to form strategic alliances or sublicense our rights to collaborators, engage with scientific advisors or hire employees or consultants, each of which would have an adverse effect on our business, results of operations and financial condition.

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

We rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information and to maintain our competitive position. Trade secrets and know-how can be difficult to protect. We seek to protect these trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, collaborators consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. We cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our product candidates that we consider proprietary. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary information will be effective.

We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. 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. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them 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 or other third party, our competitive position would be materially and adversely harmed.

If we and our partners do not adequately protect the trademarks and trade names for our products, then we and our partners may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our competitors or other third parties may challenge, infringe or circumvent the trademarks or trade names for our products. We and our partners may not be able to protect these trademarks and trade names. In addition, if the trademarks or trade names for one of our products infringe the rights of others, we or our partners may be forced to stop using the trademarks or trade names, which we need for name recognition in our markets of interest. If we cannot establish name recognition based on our trademarks and trade names, we and our partners may not be able to compete effectively and our business may be adversely affected.

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

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

- others may make drug products that are similar to AV-101 but that are not covered by the claims of our patents;
- we, or current or future strategic partners, might not have been the first to make the inventions covered by our issued patent or pending patent applications;
- we, or current or future strategic partners, might not have been the first to file patent applications covering our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- our pending and future patent applications may not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

Risks Related to Government Regulation

We may be unable to obtain regulatory approval for AV-101 under applicable regulatory requirements. The denial or delay of any such approval would delay commercialization of AV-101 and adversely impact our potential to generate revenue, our business and our results of operations.

We have not previously submitted an NDA or any other marketing application to the FDA or similar filings to comparable foreign regulatory authorities. An NDA or other similar regulatory filing requesting approval to market a product candidate must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, effective, pure and potent for each desired indication. The NDA or other similar regulatory filing must also include significant information regarding the chemistry, manufacturing and controls for the product.

The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of pharmaceutical products are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, and such regulations differ from country to country. We are not permitted to market AV-101 in the United States or in any foreign countries until it receives the requisite approval from the applicable regulatory authorities of such jurisdictions.

The FDA or any foreign regulatory bodies can delay, limit or deny approval of AV-101 for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA or the applicable foreign regulatory body that AV-101 is safe and effective for the requested indication;
- the FDA's or the applicable foreign regulatory agency's disagreement with our trial protocol or the interpretation of data from preclinical studies or clinical trials;
- our inability to demonstrate that the clinical and other benefits of AV-101 outweigh any safety or other perceived risks;
- the FDA's or the applicable foreign regulatory agency's requirement for additional preclinical studies or clinical trials;
- the FDA's or the applicable foreign regulatory agency's non-approval of the formulation, labeling or specifications of AV-101;
- the FDA's or the applicable foreign regulatory agency's failure to approve our manufacturing processes and facilities or the facilities of third-party manufacturers upon which we rely; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of pharmaceutical products in development, only a small percentage successfully complete the FDA or other regulatory bodies' approval processes and are commercialized.

Even if we eventually complete clinical testing and receive approval from the FDA or applicable foreign agencies for AV-101, the FDA or the applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. The FDA or the applicable foreign regulatory agency also may approve AV-101 for a more limited indication or a narrower patient population than we originally requested, and the FDA, or applicable foreign regulatory agency, may not approve it with the labeling that we believe is necessary or desirable for the successful commercialization.

Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of AV-101 and would materially adversely impact our business and prospects.

AV-101 is a drug-device combination product, which may result in additional regulatory risks.

Our finished drug product, a proprietary inhaled dry powder formulation and DPI, will be regulated as a drug-device combination product. The DPI we use to administer AV-101 is currently CE marked and used outside the United States but AV-101 would be the first drug to obtain approval with this DPI in the United States. We believe the delivery device we selected will work well with AV-101; however, the Phase 2b trial will be the first time we use the device in a clinical trial, and the capsules we use with the DPI in Phase 2b will be filled with higher amounts of active pharmaceutical ingredient compared to the Phase 1 trial. There may be additional regulatory risks for drug-device combination products. We may experience delays in obtaining regulatory approval of AV-101 given the increased complexity of the review process when approval of the product and a delivery device is sought under a single marketing application. In the United States, each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a drug, biologic or device. The DPI will be subject to FDA design control device requirements which comprise among other things, design verification, design validation (including human factors testing), and testing to assess performance, cleaning, and robustness. Delays in or failure of the studies conducted by us, or failure of our company, our collaborators, if any, or our third-party providers or suppliers to maintain compliance with regulatory requirements could result in increased development costs, delays in or failure to obtain regulatory approval, and associated delays in AV-101 reaching the market.

We plan to conduct clinical trials for AV-101 outside the United States, and the FDA, EMA and applicable foreign regulatory authorities may not accept data from such trials.

We plan to conduct our Phase 2b/3 clinical trial of AV-101 in PAH patients globally. The acceptance of trial data from clinical trials conducted outside the United States by the FDA, EMA, or applicable foreign regulatory authority may be subject to certain conditions. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the United States population and United States medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements.

In addition, such foreign trials will be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, EMA, or any applicable foreign regulatory authority will accept data from trials conducted outside of the United States. If the FDA, EMA, or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in AV-101 not receiving approval or clearance for commercialization in the applicable jurisdiction.

Even if we obtain regulatory approval for AV-101, we will be subject to ongoing regulatory requirements, which may result in significant additional expenses. Additionally, AV-101, if approved, could be subject to labeling and other restrictions, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with AV-101.

If AV-101 is approved by the FDA or a comparable foreign regulatory authority, it will be subject to extensive and ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the United States and requirements

of comparable foreign regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and listing, as well as continued compliance with current GMPs, and Good Manufacturing Practices, or GMPs, for any clinical trials that we conduct post-approval. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses, including the duration of use, for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. The FDA may also require a REMS in order to approve AV-101, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to current GMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with current GMP and adherence to commitments made in any approved marketing application. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

We will have to comply with requirements concerning advertising and promotion for AV-101. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we may not promote AV-101 for indications or uses for which they do not have approval. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. We also must submit new or supplemental applications and obtain approval for certain changes to AV-101, if approved, product labeling, or manufacturing process.

If we discover previously unknown problems with AV-101, such as adverse events of unanticipated severity or frequency, or problems with the facility where AV-101 is manufactured, or if the FDA disagrees with the promotion, marketing or labeling of AV-101, the FDA may impose restrictions on it or us, including requiring withdrawal of it from the market. If we fail to comply with applicable regulatory requirements, the FDA and other regulatory authorities may, among other things:

- issue warning letters or other regulatory enforcement action;
- impose injunctions, fines or civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical studies;
- refuse to approve pending applications or supplements to approved applications;
- require revisions to the labeling, including limitations on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- impose a REMS which may include distribution or use restrictions;
- require the conduct of an additional post-market clinical trial or trials to assess the safety of the product;
- impose restrictions on our operations, including closing our contract manufacturers' facilities where regulatory inspections identify observations of noncompliance requiring remediation; or
- restrict the marketing of the product, require a product recall, seizure or detention, or refuse to permit the import or export of the product.

Any government action or investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from AV-101. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

Moreover, the policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of AV-101. 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. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability.

We may seek priority review designation for AV-101, but we might not receive such designation, and even if we do, such designation may not lead to a faster regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for AV-101 for the treatment of PAH. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe AV-101 is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

We have received orphan drug designation from the FDA for AV-101 for treatment of PAH and have received a positive opinion for orphan drug designation from the EMA's Committee for Orphan Medicinal Products, but we may be unable to obtain such designations or unable to maintain the benefits associated with orphan drug status, including the potential for market exclusivity.

We have obtained orphan drug designation for AV-101 in the United States and received a positive opinion for orphan drug designation from the EMA's Committee for Orphan Medicinal Products in the European Union. We may not be able to obtain or maintain the benefits associated with orphan drug designation, including the potential for market exclusivity. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug or biologic as an orphan drug if it is a product intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population of 200,000 or more in the United States where there is no reasonable expectation that the cost of developing the product will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Similarly, in the European Union, the European Commission, upon the recommendation of the EMA's Committee for Orphan Medicinal Products, grants orphan drug designation to promote the development of drugs that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions and either (i) such condition affects not more than 5 in 10,000 persons in the European Union or (ii) without incentives, it is unlikely that the marketing of the drug in the European Union would be sufficient to justify the necessary investment in its development, and, in each case, for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or the product would be a significant benefit to those affected). In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers.

Generally, if a product with an orphan drug designation subsequently receives the first regulatory approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same product and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if, at the end of the fifth year, it is established that a product no longer meets the criteria for orphan drug designation, including if the product is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for AV-101, that exclusivity may not effectively protect AV-101 from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if

it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition or if another product with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a product nor gives the product any advantage in the regulatory review or approval process. While we may seek orphan drug designation for AV-101 from the EMA, we may never receive such designation. Even if we do receive such designation, there is no guarantee that we will enjoy the benefits of such designation.

A fast track designation by the FDA, even if granted for AV-101, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.

If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply for fast track designation by FDA for a particular indication. We may seek fast track designation AV-101, but there is no assurance that the FDA will grant this status to AV-101. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe AV-101 is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw fast track designation at any time if it believes that the designation is no longer supported by data from our clinical development program.

A breakthrough therapy designation by the FDA, even if granted for AV-101, may not lead to a faster development, regulatory review or approval process, and each designation does not increase the likelihood that AV-101 will receive regulatory approval in the United States.

We may seek a breakthrough therapy designation for AV-101 for treatment of PAH. A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug or biologic 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. Products designated as breakthrough therapies by the FDA may also be eligible for priority review and accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe AV-101 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 therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if AV-101 qualifies as a breakthrough therapy, the FDA may later decide that it no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Even if we obtain FDA approval for AV-101 in the United States, we may never obtain approval for or successfully commercialize AV-101 outside of the United States, which would limit our ability to realize its full market potential.

In order to market AV-101 outside of the United States, we must obtain marketing authorizations and comply with numerous and varying regulatory requirements of other countries regarding quality, safety and efficacy. Clinical trials conducted in one country may not be accepted by foreign regulatory authorities, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and costs for us and require additional non-clinical studies or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of AV-101 in those countries. We, as a company, do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approval in international markets is delayed, our target market for AV-101 will be reduced and we would not be able to realize the full market potential of AV-101.

Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers will be subject to applicable healthcare regulatory laws, which could expose us to penalties.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute AV-101, if approved. Such laws include, but are not limited to:

- the United States federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe, or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under any United States federal healthcare program, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. 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 False Claims Act or federal civil money penalties;
- the United States federal civil monetary penalty and civil and criminal false claims laws, including the civil federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the United States federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the United States federal government. Pharmaceutical manufacturers can cause false claims to be presented to the United States federal government by engaging in impermissible marketing practices, such as the off-label promotion of a product for an indication for which it has not received FDA approval. In addition, the government may assert that a claim including items and services resulting from a violation of the United States federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys'

fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;

- the United States Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022 (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;
- analogous United States state laws, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the United States federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state and local laws requiring the registration of pharmaceutical sales representatives;
- the United States Foreign Corrupt Practices Act of 1977, as amended, which prohibits, among other things, United States companies and their employees and agents from authorizing, promising, offering, or providing, directly or indirectly, corrupt or improper payments or anything else of value to foreign government officials, employees of public international organizations and foreign government owned or affiliated entities, candidates for foreign political office, and foreign political parties or officials thereof; and
- similar healthcare laws in the European Union and other jurisdictions, including reporting requirements detailing interactions with and payments to healthcare providers and laws governing privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of the laws described above or any other governmental laws that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from government-funded healthcare programs, such as Medicare and Medicaid or similar programs in other countries or jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment, which could affect our ability to operate our business. Further, defending against any such actions can be costly, time-consuming and may require significant personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay regulatory approval of our current or future

product candidates or any future product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell a product for which we obtain regulatory approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements, (ii) additions or modifications to product labeling, (iii) the recall or discontinuation of our products or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, or the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the United States pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower-cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. Since then, the ACA risk adjustment program payment parameters have been updated annually.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge, repeal or replace the ACA will impact our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year, and, due to subsequent legislative amendments, will remain in effect through 2030, unless additional Congressional action is taken. However, pursuant to the Coronavirus Aid, Relief and Economic Security Act, or CARES Act, and subsequent legislation, these Medicare sequester reductions have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic. In addition, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent United States Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. The likelihood of success of these and other measures initiated by the former Trump administration is uncertain, particularly in light of the new Biden administration.

Further, on May 30, 2018, 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 product candidates 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 product candidates available to eligible patients as a result of the Right to Try Act.

At the state level, individual states are increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our current or future product candidates or additional pricing pressures. In particular any policy changes through CMS as well as local state Medicaid programs could have a significant impact on our business.

Our revenue prospects could be affected by changes in healthcare spending and policy in the United States and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our current or future product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our products;
- our ability to obtain coverage and reimbursement approval for a product;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

If AV-101 is approved and we are found to have improperly promoted off-label uses of this product, we may become subject to significant liability. The FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products, if approved. In particular, while the FDA permits the dissemination of truthful and non-misleading information about an approved product, a manufacturer may not promote a product for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product's approved labeling. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined several companies from engaging in off-label promotion. The government has also imposed consent decrees, corporate integrity agreements or permanent injunctions under which specified promotional conduct must be changed or curtailed. If we cannot successfully manage the promotion of our product candidates, if approved, we could become subject to significant liability, which would materially adversely affect our business and financial condition.

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

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

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

Separately, since March 2020 when foreign and domestic inspections were largely placed on hold due to the COVID-19 pandemic, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections and resumed inspections in China and India in early 2021. In April 2021, the FDA issued guidance for industry formally announcing plans to employ remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates, and in May 2021 announced plans to continue progress toward resuming standard operational levels. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be appropriate, the agency has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. In 2020, several companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. If a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Risks Relating to Employee Matters and Managing Growth

We will need to increase the size of our organization, and we may experience difficulties in managing growth.

As of June 22, 2021, we had eight full-time employees. We will need to continue to expand our managerial, operational, finance and other resources in order to manage our operations and clinical trials, continue our development activities and commercialize AV-101. Our management and personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- effectively manage our clinical trials and the development of AV-101;
- identify, recruit, retain, incentivize and integrate additional employees, including sales personnel;
- manage our internal development and operational efforts effectively while carrying out our contractual obligations to third parties; and

- continue to improve our operational, financial and management controls, reports systems and procedures.

We may be unable to successfully implement these tasks, which could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

We are highly dependent on our key personnel and anticipate hiring new key personnel. If we are not successful in attracting and retaining highly qualified personnel, our business may be materially and adversely affected.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, as well as other members of our management team. The loss of services of any of these individuals could delay or prevent the successful development of AV-101, initiation or completion of our planned clinical trials or the commercialization of AV-101.

Competition for qualified personnel in the pharmaceutical and biotechnology fields is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

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

We have limited director and officer insurance and product liability insurance policies. Any significant insurance claims would have a material adverse effect on our business, financial condition and results of operations. Insurance availability, coverage terms, including deductibles 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.

We may be unable to adequately protect our information systems from cyberattacks, which could result in the disclosure of confidential or proprietary information, including personal data, damage our reputation, and subject us to significant financial and legal exposure.

We rely on information technology systems that we or our third-party providers operate to process, transmit and store electronic information in our day-to-day operations. In connection with our product discovery efforts, we may collect and use a variety of personal data, such as names, mailing addresses, email addresses, phone numbers and clinical trial information. A successful cyberattack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyberattacks are increasing in their frequency, sophistication, level of persistence and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives and expertise. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data security, confidentiality, integrity and availability. As a result of the COVID-19 pandemic, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. Although we devote resources to protect our information systems, we realize that cyberattacks are a threat, and there can be no assurance that our efforts will prevent information security breaches that

would result in business, legal, financial or reputational harm to us, or would have a material adverse effect on our results of operations and financial condition. Any failure to prevent or mitigate security breaches or improper access to, use of, or disclosure of our clinical data or patients' personal data could result in significant liability under state (e.g., state breach notification laws), federal, and international law and may cause a material adverse impact to our reputation, affect our ability to conduct new studies and potentially disrupt our business.

We rely on our third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches. If we or our third-party providers fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to our information technology systems, we or our third-party providers could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in the losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows. Any failure by such third parties to prevent or mitigate security breaches or improper access to or disclosure of such information could have similarly adverse consequences for us. If we are unable to prevent or mitigate the impact of such security or data privacy breaches, we could be exposed to litigation and governmental investigations, which could lead to a potential disruption to our business. By way of example, the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal data. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. In March 2020, the California State Attorney General has proposed varying versions of companion draft regulations which are not yet finalized. Despite the delay in adopting regulations, the California State Attorney General will commence enforcement actions against violators beginning July 1, 2020. The CCPA may increase our compliance costs and potential liability, and many similar laws have been proposed at the federal level and in other states.

Risks Related to Our Common Stock and This Offering

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline. Based upon the number of shares of common stock, on an as-converted basis, outstanding as of June 22, 2021, upon the completion of this offering, we will have outstanding a total of 23,108,072 shares of common stock, and assuming no exercise of the underwriters' option to purchase additional shares. Of these shares, as of the date of this prospectus, approximately 8,682,142 shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, assuming that current stockholders do not purchase shares in this offering. The representatives of the underwriters, however, may, in their sole discretion, permit our officers, directors and other stockholders who are subject to these lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, based upon the number of shares of common stock, on an as-converted basis, outstanding as of June 22, 2021, up to an additional 14,425,930 shares of common stock will be eligible for sale in the public market, 79% of which shares are held by directors, executive officers and other affiliates and will be subject to certain limitations of Rule 144 under the Securities Act of 1933, as amended, or the Securities Act.

Upon completion of this offering, 4,538,954 shares of common stock that are either subject to outstanding options or reserved for future issuance under our equity incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

After this offering, the holders of approximately 14,182,854 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market our common stock.

Our executive officers, directors, principal stockholders and their affiliates will continue to exercise significant control over our company after this offering, which will limit your ability to influence corporate matters and could delay or prevent a change in corporate control.

Immediately following the completion of this offering, and disregarding any shares of common stock that they purchase in this offering, the existing holdings of our executive officers, directors, principal stockholders and their affiliates will represent beneficial ownership, in the aggregate, of approximately 61% of our outstanding common stock, assuming no exercise of the underwriters' option to acquire additional common stock in this offering and assuming we issue the number of shares of common stock as set forth on the cover page of this prospectus. Three of our directors are affiliated with our principal stockholders, entities affiliated with RA Capital Management, L.P., Sofinnova Venture Partners X, L.P. and AtlasVenture Fund XII, L.P. As a result, these stockholders, if they act together, will be able to influence our management and affairs and control the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. These stockholders acquired their shares of common stock for substantially less than the price of the shares of common stock being acquired in this offering, and these stockholders may have interests, with respect to their common stock, that are different from those of investors in this offering and the concentration of voting power among these stockholders may have an adverse effect on the price of our common stock. In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

See the section titled "Principal Stockholders" in this prospectus for more information regarding the ownership of our outstanding common stock by our executive officers, directors, principal stockholders and their affiliates.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the initial public offering price of $14.00 per share, purchasers of common stock in this offering will experience immediate dilution of $6.49 per share in net tangible book value of the common stock. In addition, investors purchasing common stock in this offering will contribute 61% of the total amount invested by stockholders since inception but will only own 38% of the shares of common stock outstanding. In the past, we issued options and other securities to acquire common stock at prices significantly below the initial public offering price. To the extent these outstanding securities are ultimately exercised, investors purchasing common stock in this offering will sustain further dilution. See the section titled "Dilution" for a more detailed description of the dilution to new investors in the offering.

We have broad discretion in how we use the proceeds of this offering and may not use these proceeds effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering. We intend to use the net proceeds from this offering to fund discovery and clinical development efforts as well as further expansion of our manufacturing platform and capabilities, and infrastructure to support our pipeline, and to fund new and ongoing research activities, working capital and other general corporate purposes, which may include funding for the hiring of additional personnel, capital expenditures and the costs of operating as a public company. As a result, investors will be relying upon management's judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity over a three year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2020, we had federal net operating loss carryforwards of approximately $12.0 million, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to us. Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating United States federal and state taxable income. As a result, the amount of the net operating loss and tax credit carryforwards presented in our financial statements could be limited and may expire unutilized. Federal net operating loss carryforwards generated since our incorporation in July 2018 will not be subject to expiration. However, any such net operating loss carryforwards may only offset 80% of our annual taxable income in taxable years beginning after December 31, 2020.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

The rules dealing with United States federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service, or IRS, and the United States Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. For example, the TCJA was enacted in 2017 and made significant changes to corporate taxation, including the reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses from taxable years beginning after December 31, 2017 to 80% of current year taxable income and the elimination of net operating loss carrybacks generated in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), and the modification or repeal of many business deductions and credits.

Additionally, on March 27, 2020, former President Trump signed into law the Coronavirus Aid, Relief, and Economic Security Act, which, among other things, suspends the 80% limitation on the deduction for net operating losses in taxable years beginning before January 1, 2021, permits a 5-year carryback of net operating losses arising in taxable years beginning after December 31, 2017 and before January 1, 2021, and generally caps the limitation on the deduction for net interest expense at 50% of adjusted taxable income for taxable years beginning in 2019 and 2020.

The recent presidential and congressional elections in the United States could also result in significant changes in, and uncertainty with respect to, tax legislation, regulation and government policy directly affecting us and our business. For example, the United States government may enact significant changes to the taxation of business entities including, among others, a permanent increase in the corporate income tax rate, an increase in the tax rate applicable to the global intangible low-taxed income and elimination of certain exemptions, and the imposition of minimum taxes or surtaxes on certain types of income. The likelihood of these changes being enacted or implemented is unclear.

It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be promulgated or issued under existing or new tax laws, which could result in an increase in our or our stockholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

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

Our second amended and restated certificate of incorporation and amended and restated bylaws, which are to become effective at or prior to the completion of this offering, contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board of directors will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of the stockholders may be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office, and special meetings of stockholders may not be called by any other person or persons;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds (2/3) of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than a majority of all outstanding shares of our voting stock to amend any bylaws by stockholder action and not less than two-thirds (2/3) of all outstanding shares of our voting stock to amend specific provisions of our second amended and restated certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval, which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our second amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

Our amended and restated bylaws to be effective upon the consummation of this offering designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by 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 bylaws that will become effective upon the completion of this offering provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claim for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of fiduciary duty owed by any of our directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our second amended and restated certificate of incorporation or our amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or the Federal Forum Provision. In addition, our bylaws that will become effective upon the completion of this offering will provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

We recognize that the Delaware Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

General Risk Factors

Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. A global financial crisis or a global or regional political disruption could cause extreme volatility in the capital markets and lead to diminished liquidity and credit availability, declines in consumer confidence and economic growth, increases in unemployment rates and uncertainty about economic stability. For instance, the recent COVID-19 pandemic has led to a period of considerable uncertainty and volatility. A severe or prolonged economic downturn or political disruption could result in a variety of risks to our business, including weakened demand for AV-101, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or resulting in the inability of any future customers to pay for AV-101, if approved. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could adversely impact our business.

Our employees and independent contractors, including principal investigators, consultants, commercial collaborators, service providers and other vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have an adverse effect on our results of operations.

We are exposed to the risk that our employees and independent contractors, including principal investigators, consultants, any future commercial collaborators, service providers and other vendors may engage in misconduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or other unauthorized activities that violate the laws and regulations of the FDA and other similar regulatory bodies, including those laws that require the reporting of true, complete and accurate information to such regulatory bodies; manufacturing standards; United States federal and state fraud and abuse laws, data privacy and security laws and other similar non-United States laws; or laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other United States federal healthcare programs or healthcare programs in other jurisdictions, integrity oversight and reporting obligations to resolve allegations of non-compliance, imprisonment, other sanctions, contractual damages, reputational harm, diminished profits

and future earnings and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

There has been no public market for our common stock and an active, liquid and orderly market for our common stock may not develop, and you may not be able to resell your common stock at or above the public offering price.

Prior to this offering, there has been no public market for shares of our common stock. Although our common stock has been approved for listing on The Nasdaq Global Market, or Nasdaq, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price of our common stock was determined through negotiations between us and the underwriters. This initial public offering price may not be indicative of the market price of our common stock after this offering. In the absence of an active trading market for our common stock, investors may not be able to sell their common stock at or above the initial public offering price or at the time that they would like to sell.

Actual or perceived failures to comply with United States and foreign privacy and data protection laws, regulations and standards may adversely affect our business, operations and financial performance.

We are subject to or affected by numerous federal, state and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, retention, and security of personal data, such as information that we collect about patients and healthcare providers in connection with clinical trials in the United States and abroad. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, affect our or any service providers', contractors' or future collaborators' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal information, necessitate the acceptance of more onerous obligations in our contracts, result in liability or impose additional costs on us. The cost of compliance with these laws, regulations and standards is high and is likely to increase in the future. Any failure or perceived failure by us or our collaborators, service providers and contractors to comply with federal, state or foreign laws or regulation, our internal policies and procedures or our contracts governing processing of personal information could result in negative publicity, diversion of management time and effort and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising.

As our operations and business grow, we may become subject to or affected by new or additional data protection laws and regulations and face increased scrutiny or attention from regulatory authorities. In the United States, HIPAA imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, the California Consumer Privacy Act, or the CCPA, went into effect on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the United States, which could increase our potential liability and adversely affect our business. Further, on November 3, 2020, the California Privacy Rights Act, or the CPRA, was voted into law by California residents. The CPRA significantly amends the CCPA, and imposes additional data protection obligations on companies doing business in California, including additional consumer rights processes and opt outs for certain uses of sensitive data. It also creates a new California data protection agency specifically tasked to enforce the law, which would likely result in increased regulatory scrutiny of California businesses in the areas of data protection and security. The substantive requirements for businesses subject to the CPRA will go into effect on January 1, 2023, and become enforceable on July 1, 2023.

Our operations abroad may also be subject to increased scrutiny or attention from data protection authorities. Many countries in these regions have established or are in the process of establishing privacy and data security legal frameworks with which we, our collaborators, service providers, including our CRO, and contractors must comply. For example, the European Union General Data Protection Regulation, or the GDPR, went into effect in May 2018 and imposes strict requirements for processing the personal information of individuals within the European Economic Area, or the EEA, including, including clinical trial data. The GDPR

has and will continue to increase compliance burdens on us, including by mandating potentially burdensome documentation requirements and granting certain rights to individuals to control how we collect, use, disclose, retain and process information about them. The processing of sensitive personal data, such as physical health condition, may impose heightened compliance burdens under the GDPR and is a topic of active interest among foreign regulators. The GDPR also increases the scrutiny of transfers of personal data from the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws; in July 2020, the Court of Justice of the European Union limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU-US Privacy Shield and imposing further restrictions on use of the standard contractual clauses, which could increase our costs and our ability to efficiently process personal data from the EEA. In addition, the GDPR provides for more robust regulatory enforcement and fines of up to €20 million or 4% of the annual global revenue of the noncompliant company, whichever is greater. Relatedly, following the United Kingdom's withdrawal from the EEA and the EU, and the expiry of the transition period, companies will have to comply with the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the EU in relation to certain aspects of data protection law remains unclear. It is unclear how United Kingdom data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the United Kingdom will be regulated in the long term. These changes will lead to additional costs and increase our overall risk exposure. Currently there is a four to six-month grace period agreed in the EU and United Kingdom Trade and Cooperation Agreement, ending June 30, 2021 at the latest, whilst the parties discuss an adequacy decision. The European Commission published a draft adequacy decision on February 19, 2021. If adopted, the decision will enable data transfers from EU member states to the United Kingdom for a four-year period, subject to subsequent extensions.

Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators, or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations.

We are an "emerging growth company" as defined in the JOBS Act and a "smaller reporting company" as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act, and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies, which could make our common stock less attractive to investors and adversely affect the market price of our common stock.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30th. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404;
- 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;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and

- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this prospectus, we have not included all of the executive compensation-related information that would be required if we were not an emerging growth company.

Although we are still evaluating the JOBS Act, we currently intend to take advantage of some, but not all, of the available exemptions available to us so long as we qualify as an "emerging growth company." We have taken advantage of reduced reporting burdens in this prospectus. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time public companies adopt the new or revised standard.

As a result, changes in rules of United States generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an "emerging growth company," which may increase the risk that material weaknesses or significant deficiencies in our internal control over financial reporting go undetected. Likewise, so long as we qualify as an "emerging growth company," we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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.

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.

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

Our stock price is likely to be volatile. The stock market in general, and the market for biopharmaceutical companies in particular, have 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 initial public offering price. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of AV-101 or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to AV-101 and our clinical development program;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- 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;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

We will incur 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 "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq 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 these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that 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, 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 emerging growth company, 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. In additional, if we are not able to continue to meet these requirements, we may not be able to remain listed on Nasdaq.

If we fail to establish and maintain proper and effective internal control over financial reporting, our operating results and our ability to operate our business could be harmed.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be re-evaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. In connection with this offering, we intend to begin the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting. We have begun recruiting additional finance and accounting personnel with certain skill sets that we will need as a public company.

Implementing any appropriate changes to our internal controls may distract our officers and employees, entail substantial costs to modify our existing processes, and take significant time to complete. These changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate financial statements on a timely basis, could increase our operating costs and harm our business. In addition, investors' perceptions that our internal controls are inadequate or that we are unable to produce accurate financial statements on a timely basis may harm our stock price and make it more difficult for us to effectively market and sell our service to new and existing customers.

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

Upon completion of this offering, we will become subject to the periodic reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile. The stock market in general, and Nasdaq and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” and “Business,” contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the initiation, timing, progress, results and cost of our research and development program for AV-101 and our current and future clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our expectations regarding the potential market size and size of the potential patient populations for AV-101, if approved for commercial use;
- our clinical and regulatory development plans;
- our expectations with regard to the data to be derived from our planned Phase 2b/3 clinical trial;
- the timing or likelihood of regulatory filings and approvals for AV-101;
- our ability to commercialize AV-101, if approved;
- the pricing and reimbursement of AV-101, if approved;
- the implementation of our business model and strategic plans for our business and AV-101;
- estimates of our future expenses, revenues, capital requirements and our needs for additional financing, and our ability to obtain additional capital;
- the scope of protection we are able to establish and maintain for intellectual property rights covering AV-101, including the projected terms of patent protection;
- regulatory developments in the United States and foreign countries;
- our ability to enter into strategic collaborations, including for the commercialization of AV-101 outside the United States;
- the rate and degree of market acceptance of AV-101;
- our ability to contract with third-party suppliers, manufacturers and CROs and their ability to perform adequately;
- the success of competing therapies for PAH that are or may become available;
- developments relating to our competitors and our industry, including the impact of government regulation;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- our expectations related to the use of proceeds from this offering, and estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- our financial performance;
- the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our clinical trials and any future studies or trials; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

In some cases, you can identify forward-looking statements by terminology such as “may,” “should,” “could,” “goal”, “expects,” “intends,” “plans,” “anticipates,” “aims,” “believes,” “estimates,” “predicts,” “potential,”

“seeks,” “target,” “will,” “would,” “continue” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement, of which this prospectus forms a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

This prospectus also contains estimates, projections and other information concerning our industry, our business and the markets for AV-101. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this prospectus, their estimates, in particular, as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled “Risk Factors” and elsewhere in this prospectus.

The forward-looking statements contained in this prospectus are excluded from the safe harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended.

USE OF PROCEEDS

We estimate that our net proceeds from the sale of shares of our common stock in this offering will be approximately $109.9 million, or approximately $126.9 million if the underwriters exercise their option to purchase additional shares in full, based on the initial public offering price of $14.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently expect to use our net proceeds from this offering, together with our existing cash, as follows:

- Approximately $71.6 million to fund further development of AV-101 through completion of the Phase 2b portion and the data read out of the Phase 3 portion of our global Phase 2b/3 clinical trial;
- Approximately $28.1 million to fund continued chemistry, manufacturing and controls work for AV-101;
- Approximately $10.4 million to fund expenses related to pursuing a commercial launch of AV-101; and
- The remainder, if any, for working capital and general corporate purposes, which may include the hiring of additional personnel, capital expenditures and the costs of operating as a public company.

Our expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above and we expect that we will require additional funds in order to launch AV-101 in the United States, if approved by the FDA.

Based on our current plans, we believe that our existing cash, together with the anticipated net proceeds from this offering, will be sufficient for us to fund our operating expenses and capital expenditure requirements through at least into early 2025.

Due to the many inherent uncertainties in the development of AV-101 and possible additional product candidates, the amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our research and development, the timing of patient enrollment, evolving regulatory requirements, clinical trials we may commence in the future, the timing of regulatory submissions, any strategic alliances that we may enter into with third parties for AV-101 or strategic opportunities that become available to us, and any unforeseen cash needs.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation instruments, including short-term and long-term interest-bearing instruments, investment-grade securities, and direct or guaranteed obligations of the U.S. government. We cannot predict whether the proceeds invested will yield a favorable return. Our management will retain broad discretion in the application of the net proceeds we receive from our initial public offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to fund the growth and development of our business. We do not intend to pay cash dividends to our stockholders in the foreseeable future. Any future determination to declare dividends will be made at the discretion of our board of directors and will depend on our financial condition, operating results, capital requirements, general business conditions, and other factors that our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

CAPITALIZATION

The following table sets forth our cash and capitalization as of March 31, 2021.

- on an actual basis;
- on a pro forma basis to reflect (i) the issuance of 29,338,346 shares of Series A redeemable convertible preferred stock at $1.893 per share since March 31, 2021, (ii) the automatic conversion of all shares of our convertible preferred stock into an aggregate of 14,182,854 shares of our common stock and the related reclassification of the carrying value of the convertible preferred stock to permanent equity immediately prior to the closing of this offering, as if such conversion had occurred on March 31, 2021 and (iii) the filing and effectiveness of our amended and restated certificate of incorporation, which will be in effect immediately prior to the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of 8,682,142 shares of our common stock in this offering at the initial public offering price of $14.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

The pro forma and pro forma as adjusted information below is illustrative only, and our cash and capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information in conjunction with our financial statements and the related notes included in this prospectus and the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and other financial information contained in this prospectus.

	AS OF MARCH 31, 2021		
	ACTUAL	PRO FORMA	PRO FORMA AS ADJUSTED
	(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)		
Cash	$ 8,641	$ 64,178	$ 174,085
Series A redeemable convertible preferred shares, $0.0001 par value: 40,052,154 shares authorized; 10,713,808 issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	20,281	—	—
Series seed redeemable convertible preferred shares, $0.0001 par value: 4,000,000 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	4,000	—	—
Shareholders’ (deficit) equity:			
Common stock, $0.0001 par value: 50,000,000 shares authorized, 243,076 issued and outstanding, actual; 150,000,000 shares authorized, 14,425,930 issued and outstanding, pro forma; 150,000,000 shares authorized, 23,108,072 shares issued and outstanding, pro forma as adjusted	—	4	5
Additional paid-in capital	86	79,900	189,806
Accumulated deficit	(16,201)	(16,201)	(16,201)
Total shareholders’ (deficit) equity	(16,115)	63,703	173,610
Total capitalization	$ 8,166	$ 63,703	$ 173,610

The number of shares of our common stock to be outstanding after this offering on a pro forma and pro forma as adjusted basis excludes:

- 229,105 shares of common stock issuable upon the exercise of stock options outstanding under our 2018 Equity Incentive Plan, or our 2018 Plan, as of March 31, 2021, at a weighted average exercise price of $1.74 per share;
- 1,709,849 shares of common stock issuable upon the exercise of stock options outstanding under our 2018 Plan granted since March 31, 2021, at a weighted average exercise price of $2.17 per share;
- 832,000 shares of our common stock issuable upon the exercise of stock options granted in connection with this offering under our 2021 Stock Option and Incentive Plan, or our 2021 Plan, which became effective in connection with this offering, to certain of our directors, executive officers, and employees at an exercise price per share equal to the initial public offering price in this offering;
- 1,768,000 additional shares of our common stock that became available for future issuance under our 2021 Plan, as well as any future evergreen increases pursuant to the terms of the 2021 Plan; and
- 230,000 shares of our common stock that became available for future issuance under our Employee Stock Purchase Plan, or our ESPP, which became effective in connection with this offering, as well as any future evergreen increases pursuant to the terms of the ESPP.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

As of March 31, 2021, our historical net tangible book value (deficit) was $(16.1) million, or $(66.30) per share of our common stock, based on 243,076 shares of common stock issued and outstanding as of such date. Our historical net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding at March 31, 2021. Our pro forma net tangible book value as of March 31, 2021 would have been $63.7 million, or $4.42 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect the issuance of 29,338,346 shares of Series A redeemable convertible preferred stock at $1.893 per share on June 4, 2021 and to the automatic conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 14,182,854 shares of common stock prior to the completion of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of March 31, 2021, after giving effect to the pro forma adjustments described above and a 1-for-3.1060103 reverse stock split of our common stock.

After giving further effect to our issuance and sale of 8,682,142 shares of our common stock in this offering at the initial public offering price of $14.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2021 would have been $173.6 million, or $7.51 per share. This amount represents an immediate increase in pro forma as adjusted net tangible book value per share of $3.09 to our existing stockholders and immediate dilution of $6.49 in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis (without giving effect to any exercise by the underwriters of their option to purchase additional shares):

Initial public offering price per share		$ 14.00
Historical net tangible book value per share as of March 31, 2021	$(66.30)	
Increase in net tangible book value per share attributable to the pro forma adjustments described above	$ 70.72	
Pro forma net tangible book value per share as of March 31, 2021, before giving effect to this offering	$ 4.42	
Increase in pro forma net tangible book value per share attributable to investors purchasing shares in this offering	$ 3.09	
Pro forma as adjusted net tangible book value per share immediately after this offering		$ 7.51
Dilution in pro forma as adjusted net tangible book value per share to new investors purchasing shares in this offering		$ 6.49

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be $7.81 per share, representing an immediate increase in pro forma as adjusted net tangible book value per share of $0.30 to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of $6.19 to new investors purchasing common stock in this offering, based on the initial public offering price of $14.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If any shares are issued upon exercise of outstanding options, you will experience further dilution.

The following table summarizes, on the pro forma as adjusted basis described above, the differences between the number of shares of common stock purchased from us, the total consideration paid to us and the average

price per share paid by existing stockholders and by new investors purchasing shares of common stock in this offering. The calculation below is based on the initial public offering price of $14.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us:

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE PER SHARE
	NUMBER	PERCENT	AMOUNT	PERCENT	
Existing stockholders	14,425,930	62.4%	$ 79,105,029	39.4%	$ 5.48
New investors	8,682,142	37.6%	$121,549,988	60.6%	$ 14.00
Total	23,108,072	100.0%	$200,655,017	100.0%	$ 8.68

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to 59.1% of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to 40.9% of the total number of shares of our common stock outstanding after this offering.

The number of shares of our common stock to be outstanding after this offering on a pro forma and pro forma as adjusted basis excludes:

- 229,105 shares of common stock issuable upon the exercise of stock options outstanding under our 2018 Plan as of March 31, 2021, at a weighted average exercise price of $1.74 per share;
- 1,709,849 shares of common stock issuable upon the exercise of stock options outstanding under our 2018 Plan granted since March 31, 2021, at a weighted average exercise price of $2.17 per share;
- 832,000 shares of our common stock issuable upon the exercise of stock options granted in connection with this offering under our 2021 Stock Option and Incentive Plan, or our 2021 Plan, which became effective in connection with this offering, to certain of our directors, executive officers, and employees at an exercise price per share equal to the initial public offering price in this offering;
- 1,768,000 additional shares of our common stock that became available for future issuance under our 2021 Plan, as well as any future evergreen increases pursuant to the terms of the 2021 Plan; and
- 230,000 shares of our common stock that became available for future issuance under our ESPP, which became effective in connection with this offering, as well as any future evergreen increases pursuant to the terms of the ESPP.

To the extent any outstanding options or other rights are exercised, or we issue additional equity or convertible securities in the future, there will be further dilution to new investors participating in this offering.

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with our financial statements and related notes included elsewhere in this prospectus. This discussion and analysis and other parts of this prospectus contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth in the section titled "Risk Factors" and elsewhere in this prospectus. You should carefully read the "Risk Factors" section of this prospectus to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical stage biopharmaceutical company focused on developing drugs that meaningfully improve the lives of patients with rare cardiopulmonary disease. Our initial focus is on advancing AV-101, our dry powder inhaled formulation of imatinib for the treatment of pulmonary arterial hypertension, or PAH, a devastating disease impacting approximately 70,000 people in the United States and Europe. Imatinib, marketed as Gleevec tablets, was originally developed for the treatment of multiple cancers. Oral imatinib also demonstrated statistically significant improvement on the primary endpoint, six-minute walk distance, and multiple secondary hemodynamic endpoints in PAH patients in an international Phase 3 trial conducted by Novartis but was poorly tolerated due to adverse events, or AEs, and never approved for the treatment of PAH. AV-101, delivered using a dry powder inhaler, is designed to provide lung concentrations at or above those observed with the oral dose while limiting systemic levels of the drug. We have completed a Phase 1 study in healthy volunteers and AV-101 was generally well-tolerated with no serious adverse events reported. We anticipate initiating a Phase 2b/3 trial of AV-101 in PAH patients in the second half of 2021, and we have assembled a team with deep expertise in developing innovative PAH and inhaled therapies and commercializing novel drugs.

We commenced our operations in 2018 and have devoted substantially all of our resources to date to organizing and staffing our company, business planning, raising capital, meeting with regulatory authorities, developing and performing preclinical work for AV-101, preparing for and conducting our Phase 1 clinical trial of AV-101, establishing our intellectual property portfolio and providing other general and administrative support for these operations. Our operations to date have been funded primarily through the issuance of convertible preferred stock and convertible promissory notes, which were converted into Series A redeemable convertible preferred stock in August 2020. From our inception through March 31, 2021, we have raised aggregate net proceeds of $18.4 million from the issuance of convertible preferred stock and $5.0 million from the issuance of convertible promissory notes. As of March 31, 2021, we had cash of $8.6 million. On June 4, 2021, we raised aggregate net proceeds of $55.5 million from the Second Milestone Closing and Third Milestone Closing of our Series A redeemable convertible preferred stock. We believe, based on our current operating plan, that the net proceeds from this offering, together with our existing cash, will be sufficient to fund our operations into early 2025. We could use our available capital resources sooner than we currently expect, in which case we would be required to obtain additional financing, which may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. See the subsection titled "—Liquidity and Capital Resources."

We do not have any products approved for sale and have incurred significant operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future. Our net losses for the years ended December 31, 2019 and December 31, 2020 were $3.3 million and $9.6 million, respectively, and $1.4 million and $2.8 million for the three months ended March 31, 2020 and 2021, respectively. As of March 31, 2021, we had an accumulated deficit of $16.2 million. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical development activities, other research and development activities and pre-commercialization activities. We expect to continue to incur significant expenses and increasing operating losses into the foreseeable future. We anticipate our expenses will increase substantially as we continue our research and development activities,

including the clinical development of AV-101, seek regulatory approval for and potentially commercialize AV-101, as well as hire additional personnel, protect our intellectual property, and incur additional costs associated with being a public company.

We do not expect to generate any revenue from product sales unless and until we successfully complete development and obtain regulatory approval for AV-101 or any other drug candidate, which will not be for at least the next several years, if ever. In addition, if we obtain regulatory approval for AV-101, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, until such time as we can generate significant revenue from sales of AV-101, if ever, we expect to finance our cash needs through a combination of equity offerings, debt financings, or other capital sources, including potential collaborations and licenses and other similar arrangements. However, we may not be able to secure additional financing or enter into such other arrangements in a timely manner or on favorable terms, if at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional capital when needed, we could be forced to delay, limit, reduce or terminate our research and development programs or future commercialization efforts, or grant rights to develop and market AV-101 even if we would otherwise prefer to develop and market such drug candidate ourselves.

We do not own or operate manufacturing facilities. We currently rely on third-party manufacturers and suppliers for our drug candidate, and we expect to continue to do so to meet our preclinical, clinical and potential commercial activities. Our third-party manufacturers are required to manufacture our drug candidate under current good manufacturing practice, or current GMP, requirements and other applicable laws and regulations. We believe there are multiple sources for all of the materials required for the manufacture of AV-101, and we expect to continue to cost-effectively produce drug candidates at contract manufacturing facilities.

The global coronavirus disease 2019, or COVID-19, pandemic continues to evolve, and we will continue to monitor the COVID-19 situation. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain, and will depend on certain developments, including the duration and spread of the outbreak and its impact on our clinical trial enrollment, trial sites, contract research organizations (CROs), third-party manufacturers, and other third parties with whom we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. To the extent possible, we are conducting business as usual, with only necessary or advisable modifications to employee travel. We currently do not lease any facilities as our entire organization works remotely. We plan to lease office space in the greater Boston, Massachusetts metropolitan area. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with whom we do business. At this point, the extent to which the COVID-19 pandemic may affect our business, operations and clinical development timelines and plans, including the resulting impact on our expenditures and capital needs, remains uncertain and is subject to change.

Components of Results of Operations

Revenue

We currently have no products approved for sale, and we have not generated any revenue to date. In the future, we may generate revenue from collaboration or license agreements we may enter into with respect to our drug candidate, as well as product sales from any approved product, which approval we do not expect to occur for at least the next several years, if ever. Our ability to generate product revenue will depend on the successful development and eventual commercialization of AV-101 and any other drug candidates we may pursue. If we fail to complete the development of AV-101 in a timely manner, or to obtain regulatory approval, our ability to generate future revenue and our results of operations and financial position would be materially adversely affected.

Operating Expenses

Research and Development

To date, our research and development expenses have related to the development of AV-101. Research and development expenses are recognized as incurred and payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received.

Research and development expenses include:

- external research and development expenses incurred under agreements with contract research organizations, or CROs, and consultants to conduct and support clinical trials of AV-101 and our preclinical studies;
- costs related to manufacturing AV-101 for use in clinical trials; and
- personnel-related costs, including salaries, payroll taxes, employee benefits, and stock-based compensation charges for those individuals involved in research and development efforts.

Our research and development expenses consist principally of direct costs, such as fees paid to CROs, investigative sites and consultants in connection with our clinical trials, preclinical and non-clinical studies, and costs related to manufacturing clinical trial materials. We deploy our personnel related resources across all of our research and development activities. We track direct expenses on a clinical and non-clinical basis.

We plan to substantially increase our research and development expenses for the foreseeable future as we continue the development of AV-101. We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future clinical trials and nonclinical studies of AV-101 or any future product candidates due to the inherently unpredictable nature of clinical and preclinical development. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We will need to raise substantial additional capital in the future.

Our future clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses evaluated in the trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up; and
- the efficacy and safety profile of the product candidate.

General and Administrative

General and administrative expenses consist primarily of personnel-related costs, including salaries, payroll taxes, employee benefits, and stock-based compensation charges for those individuals in executive, finance and other administrative functions. Other significant costs include legal fees relating to intellectual property and corporate matters, professional fees for accounting and consulting services, and insurance costs. We anticipate that our general and administrative expenses will increase for the foreseeable future to support our continued research and development activities, pre-commercial preparation activities and commercialization activities for AV-101. We also anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Interest Expense

For the years ended December 31, 2019 and 2020 and for the three months ended March 31, 2020 and 2021, interest expense consisted of interest on our convertible promissory notes at a per annum interest rate

of 6%. All convertible promissory notes converted into shares of our Series A redeemable convertible preferred stock in August 2020.

Change in Fair Value of Convertible Promissory Notes

We issued convertible promissory notes in 2019 and 2020 for which we elected the fair value option. We adjusted the carrying value of our convertible promissory notes to their estimated fair value at each reporting date, with any change in fair value of the convertible promissory notes recorded as an increase or decrease to change in fair value of convertible promissory notes in our statements of operations and comprehensive loss. All convertible promissory notes and related accrued interest converted into shares of Series A redeemable convertible preferred stock in August 2020.

Prior to their conversion into our Series A redeemable convertible preferred stock issued in August 2020, the fair value of convertible promissory notes issued through July 2020 was estimated using a scenario-based analysis that estimated the fair value of the convertible promissory notes based on the probability-weighted present value of expected future investment returns, considering possible outcomes available to the noteholders, including conversions in subsequent equity financings, change of control transactions, settlement and dissolution.

Results of Operations

Comparison of the Three Months Ended March 31, 2020 and 2021 (Unaudited)

The following table summarizes our results of operations for the three months ended March 31, 2020 and 2021 (in thousands):

	THREE MONTHS ENDED MARCH 31,		
	2020	2021	CHANGE
	(UNAUDITED)		
Operating expenses:			
Research and development	$ 1,206	$ 2,196	$ 990
General and administrative	152	584	432
Total operating expenses	1,358	2,780	1,422
Loss from operations	(1,358)	(2,780)	(1,422)
Other expense:			
Interest expense	(38)	—	38
Change in fair value of convertible promissory notes	(40)	—	40
Other expense	—	(1)	(1)
Total other expense	(78)	(1)	77
Net loss and comprehensive loss	$ (1,436)	$ (2,781)	$ (1,345)

Research and Development Expenses

Research and development expenses for the three months ended March 31, 2020 were $1.2 million compared to $2.2 million for the three months ended March 31, 2021. The increase of $1.0 million was primarily due to increases of $0.5 million in clinical, $0.1 million in regulatory costs, $0.4 million in clinical manufacturing costs and $0.3 million in payroll, stock-based compensation, and professional fees partially offset by lower pre-clinical related costs of $0.3 million.

General and Administrative Expenses

General and administrative expenses for the three months ended March 31, 2020 were $0.2 million compared to $0.6 million for the three months ended March 31, 2021. The increase of $0.4 million was primarily due to increases of $0.2 million in professional services related to corporate legal fees, accounting services and other consulting expenses and $0.2 million in payroll and recruiting fees.

Other Expense

Other expense for the three months ended March 31, 2020 was $0.1 million compared to $988 of other expense for the three months ended March 31, 2021. The change of $0.1 million was due to the change in fair value of the convertible promissory notes expense and interest expense on the convertible promissory notes.

Comparison of the Years Ended December 31, 2019 and 2020

The following table summarizes our results of operations for the years ended December 31, 2019 and 2020 (in thousands):

	YEARS ENDED DECEMBER 31,		
	2019	2020	CHANGE
Operating expenses:			
Research and development	$ 3,112	$ 7,940	$ 4,828
General and administrative	218	949	731
Total operating expenses	3,330	8,889	5,559
Provision for income taxes	1	—	(1)
Loss from operations	(3,331)	(8,889)	(5,558)
Other income (expense):			
Interest expense	—	(75)	(75)
Change in fair value of convertible promissory notes	—	(644)	(644)
Other income (expense)	1	(3)	(4)
Total other income (expense)	1	(722)	(723)
Net loss and comprehensive loss	$ (3,330)	$ (9,611)	$ (6,281)

Research and Development Expenses

Research and development expenses for the year ended December 31, 2019 were $3.1 million compared to $7.9 million for the year ended December 31, 2020. The increase of $4.8 million was primarily due to increases of $2.0 million in clinical costs, $0.4 million in regulatory costs, $2.4 million in manufacturing costs and $0.4 million in payroll, stock-based compensation, and professional fees partially offset by lower pre-clinical related costs of $0.4 million.

General and Administrative Expenses

General and administrative expenses for the year ended December 31, 2019 were $0.2 million compared to $0.9 million for the year ended December 31, 2020. The increase of $0.7 million was primarily due to increases of $0.4 million in professional services related to corporate legal fees, accounting services and other consulting expenses and $0.3 million in payroll, stock-based compensation and professional fees.

Other Income (Expense)

Other income for the year ended December 31, 2019 was $1,221 compared to $0.7 million of other expense for the year ended December 31, 2020. The change of $0.7 million for the year ended December 31, 2020 was due to the change in fair value of the convertible promissory notes expense and interest expense on the convertible promissory notes being recorded in 2020, as the convertible promissory notes were issued at fair value in December 2019 and no interest expense was recorded in 2019.

Liquidity and Capital Resources

We have incurred significant operating losses since our inception and anticipate we will continue to incur significant operating losses for the foreseeable future as we continue to develop AV-101 and may never become profitable. As of March 31, 2021, we had cash of $8.6 million and an accumulated deficit of $16.2 million.

Convertible Preferred Stock Financings

Since our inception, we have funded our operations primarily through the private placement of our convertible preferred stock. From inception through March 31, 2021, we received net proceeds of $4.0 million and

$14.4 million from the issuance of shares of our Series Seed redeemable convertible preferred stock and Series A redeemable convertible preferred stock, respectively.

Convertible Promissory Note Financings

From December 2019 to July 2020, we issued an aggregate of $5.0 million of convertible promissory notes to related parties. In August 2020, these convertible promissory notes and related accrued interest were converted, at their then fair value, into 3,020,998 shares of our Series A redeemable convertible preferred stock.

Future Funding Requirements

We have prepared operating plans and cash flow forecasts which indicate that the $55.5 million of proceeds received from the Second Milestone Closing and Third Milestone Closing of the Series A redeemable convertible preferred stock received on June 4, 2021 in addition to existing cash on-hand will be sufficient to fund our operations for at least 12 months from the date these unaudited condensed financial statements as of and for the three months ended March 31, 2021 are issued. Our independent registered public accounting firm included an explanatory paragraph in its report on our financial statements as of and for the year ended December 31, 2020 indicating that there is substantial doubt about our ability to continue as a going concern. The substantial doubt about our ability to continue as a going concern raised in connection with the financial statements as of and for the year ended December 31, 2020 did not factor in the proceeds received on June 4, 2021 from the Second Milestone Closing and Third Milestone Closing of our Series A redeemable convertible preferred stock.

Based on our current operating plan, we believe that our existing cash, proceeds from our Series A redeemable convertible preferred milestone closings, together with the estimated net proceeds from this offering, will be sufficient to fund our operations into early 2025. In particular, we expect the net proceeds from this offering will allow us to continue our development of AV-101. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our capital resources sooner than we expect. Additionally, the process of conducting clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

Our future capital requirements will depend on many factors, including:

- the type, number, scope, results, costs and timing of preclinical studies and clinical trials of AV-101, including changes to our development plan based on feedback received from regulatory authorities, and preclinical studies or clinical trials of other potential drug candidates or indications we may choose to pursue in the future;
- the costs and timing of manufacturing for AV-101 or any other product candidates, including commercial scale manufacturing;
- the costs, timing and outcome of regulatory review of AV-101 or any other drug candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting;
- the costs associated with hiring additional personnel and consultants as our business grows, including additional clinical development personnel;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- the timing and amount of the milestone or other payments we must make to any future licensors, if we enter into any license agreements;
- the costs and timing of establishing or securing sales and marketing capabilities if AV-101 or any other product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third- party payors and adequate market share and revenue for any approved products;

- patients' willingness to pay out-of-pocket for any approved products in the absence of coverage and/or adequate reimbursement from third-party payors; and
- costs associated with any products or technologies that we may in-license or acquire.

Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, potentially including collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or drug candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. Our failure to raise capital or enter into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our drug candidates even if we would otherwise prefer to develop and market such drug candidates ourselves.

Cash Flows

Comparison of the Three Months Ended March 31, 2020 and 2021 (Unaudited)

The following table sets forth a summary of the net cash flow activity for the three months ended March 31, 2020 and 2021 (in thousands):

	THREE MONTHS ENDED MARCH 31,	
	2020	2021
	(UNAUDITED)	
Net cash used in operating activities	$ (1,183)	$ (3,775)
Net cash used by investing activities	—	(40)
Net cash provided by financing activities	—	7,883
Net (decrease) increase in cash	$ (1,183)	$ 4,068

Operating Activities

Net cash used in operating activities for the three months ended March 31, 2021 was $3.8 million consisting primarily of our net loss incurred during the period of $2.8 million adjusted for $1.0 million for net changes in operating assets and liabilities. The net change in operating assets and liabilities primarily related to a $0.9 million increase in prepaid expenses and other current assets and a $0.1 million decrease in accounts payable and accrued and other current liabilities in support of the growth in our operating activities.

Net cash used in operating activities for the three months ended March 31, 2020 was $1.2 million, consisting primarily of our net loss incurred during the period of $1.4 million adjusted for $0.1 million of noncash charges and $0.1 million for net changes in operating assets and liabilities. Noncash charges consisted of $0.1 million in change in fair value of convertible promissory notes to related party and non-cash interest expense. The net change in operating assets and liabilities related to a $0.2 million increase in accounts payable and accrued and other current liabilities partially offset by a $0.1 million increase in prepaid and other current assets in support of the growth in our operating activities.

Investing Activities

Net cash used in investing activities for the three months ended March 31, 2021 was $40,000 due to purchases of property and equipment to support our research activities.

Financing Activities

Net cash provided by financing activities for the three months ended March 31, 2021 was $7.9 million due to $8.0 million in net proceeds received from the sale of Series A redeemable convertible preferred stock, net of issuance of costs, partially offset by $0.1 million of deferred offering costs for the planned initial public offering.

Comparison of the Years Ended December 31, 2019 and 2020

The following table sets forth a summary of the net cash flow activity for the years ended December 31, 2019 and 2020 (in thousands):

	YEARS ENDED DECEMBER 31,	
	2019	2020
Net cash used in operating activities	$ (2,781)	$ (7,859)
Net cash provided by financing activities	2,500	8,918
Net (decrease) increase in cash	$ (281)	$ 1,059

Operating Activities

We have incurred significant operating losses since inception. Net cash used in operating activities for the year ended December 31, 2020 was $7.9 million, consisting primarily of our net loss incurred during the period of $9.6 million adjusted for $0.8 million of noncash charges and $0.9 million for net changes in operating assets and liabilities. Noncash charges consisted primarily of $0.6 million in change in fair value of convertible promissory notes to related party. The net change in operating assets and liabilities related to a $1.0 million increase in accounts payable and accrued and other current liabilities partially offset by a $0.1 million increase in prepaid and other current assets in support of the growth in our operating activities.

Net cash used in operating activities for the year ended December 31, 2019 was $2.8 million consisting primarily of our net loss incurred during the period of $3.3 million adjusted for $0.5 million for net changes in operating assets and liabilities. The net change in operating assets and liabilities primarily related to a $0.5 million increase in accounts payable and accrued and other current liabilities in support of the growth in our operating activities.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2020 was $8.9 million, primarily related to $6.4 million in net proceeds received from the sale of Series A redeemable convertible preferred stock and through the issuance and conversion of $2.5 million of convertible promissory notes to related parties issued in July 2020.

Net cash provided by financing activities for the year ended December 31, 2019 was $2.5 million and was due to $2.5 million in net proceeds received from the issuance of convertible promissory notes to related parties in December 2019, which subsequently converted into Series A redeemable convertible preferred stock in August 2020.

Contractual Obligations and Commitments

As of March 31, 2021, we do not have any long-term debt obligations, capital lease obligations, operating lease obligations, purchase obligations or long-term liabilities.

We enter into contracts in the normal course of business for contract research services, contract manufacturing services, professional services and other services and products for operating purposes. These contracts generally provide for termination after a notice period, and, therefore, are cancelable contracts and not included above.

Critical Accounting Policies and Significant Judgments and Estimates

Our financial statements are prepared in accordance with generally accepted accounting principles in the United States (GAAP). The preparation of our financial statements requires us to make estimates and

assumptions that affect the reported amounts of assets, liabilities, costs, and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. We base our estimates and assumptions on historical experience and other factors that we believe to be reasonable under the circumstances. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 1 to our financial statements appearing elsewhere in this prospectus, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Research and Development Expenses and Accrued Research and Development Costs

We are required to estimate our expenses resulting from obligations under contracts with vendors, consultants and CROs, in connection with conducting research and development activities. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. We reflect research and development expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of the preclinical or clinical study as measured by the timing of various aspects of the study or related activities. We determine accrual estimates through review of the underlying contracts along with preparation of financial models taking into account discussions with research and other key personnel as to the progress of studies, or other services being conducted. During the course of a study, we adjust our rate of expense recognition if actual results differ from our estimates.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Fair Value Convertible Promissory Notes

As described above, convertible promissory notes are revalued at each reporting period with changes in the fair value of the liabilities recorded as a component of other expense in the statement of operations and comprehensive loss. There are significant judgments and estimates inherent in the determination of the fair value of these liabilities. If we had made different assumptions including, among others, those related to the timing and probability of various corporate scenarios and discount rates, the carrying values of our convertible promissory notes and our net loss and net loss per common share could have been significantly different.

Stock-Based Compensation Expense

Stock-based compensation expense represents the cost of the grant date fair value of employee and non-employee stock options. We estimate the fair value of stock options on the date of grant using the Black-Scholes option pricing model and recognize the expense over the requisite service period of the awards, which is generally the vesting period, on a straight-line basis. We account for forfeitures when they occur and reverse any compensation cost previously recognized for awards for which the requisite service has not been completed, in the period that the award is forfeited.

The Black-Scholes option pricing model uses inputs which are highly subjective assumptions and generally require significant judgment. These assumptions include:

- *Fair Value of Common Stock*. See the subsection titled "—Common Stock Valuations" below.
- *Expected Term*. The expected term represents the period that the options granted are expected to be outstanding. The expected term of stock options issued is determined using the simplified method (based on the average of the vesting term and the original contractual term) as we have concluded that our stock option exercise history does not provide a reasonable basis upon which to estimate expected term.

- *Expected Volatility*. Given that our common stock is privately held, there is no active trading market for our common stock. We derived the expected volatility from the average historical volatilities over a period approximately equal to the expected term of comparable publicly traded companies within our peer group that were deemed to be representative of future stock price trends as we have limited trading history for our common stock. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.
- *Risk-Free Interest Rate*. The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of options.
- *Expected Dividend Yield*. We have never paid dividends on our common stock and do not anticipate paying any dividends in the foreseeable future. Therefore, we used an expected dividend yield of zero.

See Note 7 to our audited financial statements included elsewhere in this prospectus for more information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options. Certain of such assumptions involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our stock-based compensation could be materially different.

We recorded no stock-based compensation expense for the year ended December 31, 2019 and $0.1 million of stock-based compensation expense for the year ended December 31, 2020. We recorded stock-based compensation expense for the three months ended March 31, 2020 and 2021 of $6,833 and $23,557, respectively. As of March 31, 2021, there was $0.2 million of total unrecognized stock-based compensation expense related to unvested stock options which we expect to recognize over a remaining weighted-average period of 2.9 years. We expect to continue to grant stock options and other equity-based awards in the future, and to the extent that we do, our stock-based compensation expense recognized in future periods will likely increase.

The intrinsic value of all outstanding options as of March 31, 2021 was $2.8 million based on the initial public offering price of $14.00 per share, of which approximately $0.3 million was related to vested options and approximately $2.5 million was related to unvested options.

Common Stock Valuations and Stock Option Grants

We are required to estimate the fair value of the common stock underlying our stock-based awards when performing fair value calculations using the Black-Scholes option pricing model. Because our common stock is not currently publicly traded, the fair value of the common stock underlying our stock-based awards has been determined on each grant date by our board of directors, with input from management, considering our most recently available third-party valuation of common shares. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant.

Our determination of the value of our common stock was performed using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants, or AICPA, *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the AICPA Practice Aid. In addition, our board of directors considered various objective and subjective factors to determine the fair value of our common stock, including:

- valuations of our common stock performed by independent third-party valuation specialists;
- the anticipated capital structure that will directly impact the value of the currently outstanding securities;
- our results of operations and financial position;
- the status of our research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;

- external market conditions affecting the life sciences and biotechnology industry sectors;
- U.S. and global economic conditions;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an IPO or a sale of our company, given prevailing market conditions; and
- the market value and volatility of comparable companies.

The AICPA Practice Aid identifies various available methods for allocating enterprise value across classes and series of capital stock to determine the estimated fair value of common stock at each valuation date. In accordance with the Practice Aid, we considered the following methods:

- *Option Pricing Method (OPM)*. Under the OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options. This method is appropriate to use when the range of possible future outcomes is so difficult to predict that estimates would be highly speculative, and dissolution or liquidation is not imminent.
- *Probability-Weighted Expected Return Method (PWERM)*. The PWERM is a scenario-based analysis that estimates value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.
- *Hybrid Method*. The hybrid method is a PWERM where the equity value in one or more scenarios is calculated using an OPM.

Based on our early stage of development, the difficulty in predicting the range of specific outcomes (and their likelihood) and other relevant factors, we determined that an OPM was the most appropriate method for allocating our enterprise value to determine the estimated fair value of our common stock for valuation dates through 2020. In order to determine the fair value of our common stock on a marketable basis, we then applied a discount for lack of marketability which we derived based on inputs including a company-specific volatility rate, a term equal to the expected time to a future liquidity event and a risk-free rate equal to the yield on treasuries of similar duration.

In 2021, we incorporated the Hybrid Method into the valuation process as a result of the increasing likelihood of the occurrence of certain discrete events, such as an initial public offering, which is a result of improving market conditions and receptivity of the market to initial public offerings. In the PWERM, we established our enterprise value utilizing a valuation multiple based on precedent initial public offerings and our recent financing rounds. The enterprise value determined under the PWERM and OPM was weighted according to management's estimate of the probability of the occurrence of a potential initial public offering as of the valuation date. The resulting equity value for our common stock was then determined by taking the per share value from each approach and applying their respective weightings to arrive at a per share value on a non-marketable basis. In order to determine the fair value of our common stock on a marketable basis, we then applied a discount for lack of marketability which we derived based on inputs including a company-specific volatility rate, a term equal to the expected time to a future liquidity event and a risk-free rate equal to the yield on treasuries of similar duration.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event and the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been significantly different.

The following table sets forth by grant date the number of shares subject to stock options granted from February 14, 2020, the date we first granted options, through June 2, 2021, the per share exercise price of options, the fair value of common stock per share on each grant date, and the per share estimated fair value of options:

GRANT DATE	NUMBER OF SHARES SUBJECT TO OPTIONS GRANTED	PER SHARE EXERCISE PRICE OF OPTIONS[1]	FAIR VALUE PER COMMON SHARE ON GRANT DATE[1]	PER SHARE ESTIMATED FAIR VALUE OF OPTIONS[2]
February 14, 2020[3]	48,293	$ 1.74	$ 1.74	(3)
May 1, 2020[3]	16,097	$ 1.74	$ 1.74	(3)
May 19, 2020[3]	16,097	$ 1.74	$ 1.74	(3)
September 4, 2020	142,186	$ 1.74	$ 1.74	$ 1.09
November 24, 2020	8,041	$ 1.74	$ 1.74	$ 1.09
April 2, 2021	1,701,543	$ 2.14	$ 2.14	(4)
June 2, 2021	8,306	$ 7.67	$ 7.67	(4)

(1) The per share exercise price of options represents the fair value of our common stock on the date of grant, as determined by our board of directors, after taking into account our most recently available contemporaneous valuation of our common stock as well as additional factors that may have changed since the date of such contemporaneous valuation through the date of grant.

(2) The per share estimated fair value of options reflects the weighted average fair value of options granted on each grant date, determined using the Black-Scholes option pricing model.

(3) These options were granted at a Per Share Exercise Price and Fair Value per Common Share on Grant Date of $2.95 and were subsequently modified on September 4, 2020 to change the per share exercise price to $1.74.

(4) We intend to determine our compensation expense relating to the April 2, 2021 and June 2, 2021 awards in connection with our preparation and review of our unaudited financial statements for the period ending June 30, 2021. Once determined, our estimate of the grant date fair value of these share-based awards will be reflected in the financial statements relating to such period.

Following the closing of this offering, the fair value of our common stock will be equal to the closing price of our common stock as reported on the date of the grant.

Internal Control Over Financial Reporting

Pursuant to Section 404(a) of the Sarbanes-Oxley Act of 2002, as amended, commencing the year following our first annual report required to be filed with the SEC, our management will be required to report on the effectiveness of our internal control over financial reporting. To comply with the requirements of being a reporting company under the Exchange Act, we will need to implement additional financial and management controls, reporting systems and procedures and hire additional accounting and finance staff, as well as potentially upgrade our information technology systems.

Emerging Growth Company Status

As an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, we can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to “opt out” of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time public companies adopt the new or revised standard. The decision to opt out of the extended transition period under the JOBS Act is irrevocable.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Recently Adopted Accounting Pronouncements

See Note 1 to of our financial statements appearing elsewhere in this prospectus.

BUSINESS

Overview

We are a clinical stage biopharmaceutical company focused on developing drugs that meaningfully improve the lives of patients with rare cardiopulmonary disease. Our initial focus is on advancing AV-101, our dry powder inhaled formulation of imatinib for the treatment of pulmonary arterial hypertension, or PAH, a devastating disease impacting approximately 70,000 people in the United States and Europe. Imatinib, marketed as Gleevec tablets, was originally developed for the treatment of multiple cancers. Oral imatinib also demonstrated statistically significant improvement on the primary endpoint, six-minute walk distance, and multiple secondary hemodynamic endpoints in PAH patients in an international Phase 3 trial conducted by Novartis but was poorly tolerated due to adverse events, or AEs, and never approved for the treatment of PAH. AV-101, delivered using a dry powder inhaler, is designed to provide lung concentrations at or above those observed with the oral dose while limiting systemic levels of the drug. We have completed a Phase 1 study in healthy volunteers and AV-101 was generally well-tolerated with no serious adverse events reported. We anticipate initiating a Phase 2b/3 trial of AV-101 in PAH patients in the second half of 2021, and we have assembled a team with deep expertise in developing innovative PAH and inhaled therapies and commercializing novel drugs.

PAH is an orphan disease with unmet medical need and is characterized by high pressure in the vessels transporting blood from the right side of the heart to the lungs. This high pressure is caused by abnormal cellular proliferation, which over time results in narrowing of the pulmonary vessels and forces the heart to work harder to pump blood through the lungs. The severe blood flow restriction and strain on the heart becomes increasingly severe over time and ultimately leads to heart failure that is often fatal. We estimate there are between 30,000-40,000 patients treated with approved PAH therapies in the U.S. alone, many of whom are on two or more approved PAH therapies. It is estimated that the combined global sales for PAH products in 2020 was $5.4 billion. Despite the availability of multiple approved therapies, PAH has a five-year life expectancy for newly diagnosed and prevalent patients between 61% and 65%. None of the approved therapies directly address the abnormal cellular proliferation of the pulmonary vasculature that causes the increased resistance to blood flow. We believe that novel treatments that primarily address abnormal cellular proliferation may provide therapeutic benefit to PAH patients and lead to improved quality of life.

Our focus on developing AV-101 is driven by historical results from the Phase 3 IMPRES clinical trial of oral imatinib for the treatment of PAH patients. Oral imatinib is a well-characterized targeted kinase inhibitor and approved oncology treatment, but clinical trials also supported its potential for the treatment of PAH. The Phase 3 IMPRES trial was a placebo-controlled clinical trial of oral imatinib, conducted globally by Novartis, in 202 PAH patients whose disease was not adequately controlled by two or all three classes of approved PAH therapies. After 24 weeks of treatment with oral imatinib, patients achieved on average an increase of 32 meters ($p=0.002$) compared to placebo in the distance they could walk in six minutes, a measure known as the 6MWD. A key secondary endpoint in the IMPRES trial was pulmonary vascular resistance, or PVR, which is an objective measure of hemodynamic disease severity in PAH patients. After 24 weeks of treatment with oral imatinib, patients achieved an average PVR improvement (reduction) of 32% ($p<0.001$) compared to placebo with a significant increase in cardiac output ($p<0.001$). The magnitude of improvement in both 6MWD and PVR is notable because no other PAH drug has shown such an improvement in a Phase 3 trial on top of at least two background therapies. However, treatment with oral imatinib was also associated with significant tolerability issues and adverse events, including nausea, edema, diarrhea and vomiting. Patients taking oral imatinib also experienced serious adverse events, the most frequent of which were anemia (7%), worsening of pulmonary hypertension (6%), dyspnea (6%), peripheral edema (6%), presyncope (5%), diarrhea (3%), device-related infection (3%), subdural hematoma (2%) and syncope (1%). Despite the clinical effects of oral imatinib 26% of patients on oral imatinib, compared to 7% on placebo, discontinued due to AEs by 24 weeks.

Our company was formed to develop an inhaled formulation of imatinib as a means of delivering therapeutically relevant drug concentrations to the lungs while minimizing systemic and gastrointestinal exposure, which we believe are the sources of the observed intolerability of oral imatinib. We have brought together leaders both in the field of PAH drug development as well as in the area of inhaled drug formulation to invent AV-101, a drug/device combination designed to deliver imatinib directly to the lungs.

We have completed a Phase 1 trial of AV-101 in 82 healthy adults. Repeat inhaled doses of up to 90 mg were well-tolerated and resulted in systemic plasma levels that were below those observed with the 400 mg oral dose of imatinib (Gleevec) used in the IMPRES trial. According to pharmacokinetic models of lung exposure to imatinib as applied to our Phase 1 dose range, the predicted lung concentrations of imatinib delivered by AV-101 overlapped or surpassed those predicted from the 400 mg dose of oral imatinib in our Phase 1 trial. There were no serious adverse events associated with AV-101. The most common adverse event was a transient cough, which was generally mild, and resolved within 30 minutes of dosing. There were no discontinuations due to cough. The intended Phase 2b dose range with AV-101 will only include doses that use 40% or less of the amount of dry powder that was inhaled at the highest Phase 1 dose and, based on the results of our Phase 1 trial and our modeling, we expect lung concentrations of imatinib delivered by AV-101 in the 35 mg and 70 mg doses, both twice a day, or BID, selected for the Phase 2b portion of our Phase 2b/3 trial to overlap or surpass the lung concentrations predicted with the 400 mg oral dose in our Phase 1 trial, which was the same target dose used in the Phase 3 IMPRES trial.

We anticipate initiating a global double-blinded, placebo-controlled, randomized Phase 2b/3 trial of AV-101 in the second half of 2021 in PAH patients taking at least two background therapies. The Phase 2b portion of this trial will enroll approximately 200 PAH patients and is designed to assess safety, tolerability and inform dose selection for the Phase 3 portion using changes in PVR, an objective measure of the effect of AV-101 on hemodynamic function in PAH patients, as the primary endpoint. We will measure 6MWD as a secondary endpoint in the Phase 2b portion of this trial. We anticipate that topline data from the Phase 2b portion of this trial will be available in the middle of 2023. In the Phase 3 portion of the trial improvement in 6MWD will be the primary endpoint. If the results of the Phase 3 trial show a statistically significant increase in 6MWD, we plan to submit a New Drug Application, or NDA, with the United States Food and Drug Administration, or FDA, and Marketing Authorization Application, or MAA, with the EMA for AV-101 for the treatment of PAH. These applications will leverage the existing safety data for Gleevec oral tablets allowing the company to save time and money. If AV-101 is approved, we believe it has the potential to become an important addition to existing therapies for PAH in both the United States and Europe.

We are pursuing a clinical development program utilizing established endpoints for development of previous PAH drugs, as well as enrollment criteria and dosing duration previously studied in oral imatinib PAH trials. At our April 14, 2021 end-of-Phase 1 meeting with the FDA, we received regulatory guidance that our clinical program could support a NDA submission; however, the process of clinical development is inherently uncertain and there can be no guarantee that we will obtain marketing approval. AV-101 has been granted orphan drug designation by the FDA for the treatment of PAH. We have filed for patent protection of the composition of the aerosol, drug product, manufacturing and methods of use. We retain worldwide commercial rights to AV-101.

Our Team and Investors

Our executive management team has extensive experience in the clinical development and the commercialization of orphan drug indications. Timothy P. Noyes, our Chief Executive Officer, was a senior executive at GelTex Pharmaceuticals, Inc., or GelTex, and Genzyme Corporation, or Genzyme, where he headed all launch planning and the commercialization of Renagel, a treatment for hemodialysis patients that resulted in Genzyme's acquisition of GelTex for more than $1 billion. Benjamin T. Dake, Ph.D., our Founder, President, Chief Operating Officer and Secretary, a cancer biologist, investor and entrepreneur, recognized the potential benefits of developing a lung-targeted imatinib and secured multiple rounds of funding to build the team at Aerovate with experts like Ralph Niven, Ph.D., our Chief Development Officer, who has 25 years of expertise in translational medicine and inhalation dosage forms, and Hunter Gillies, M.B.Ch.B., our Chief Medical Officer, who has led Phase 2 and Phase 3 PAH trials at Pfizer Inc., or Pfizer, and Gilead Sciences, Inc., or Gilead, and has designed and executed PAH trials with several smaller biotechnology companies. George A. Eldridge, our Chief Financial Officer, has served as CFO for several biotechnology companies, leading four of these companies to the public markets.

We have received approximately $79.1 million in financing. Our Series A financing round was led by Sofinnova Investments, with participation from Atlas Venture, Cormorant Asset Management, Surveyor Capital (a Citadel company), Osage Venture Partners and RA Capital. RA Capital seeded and launched Aerovate in 2018.

Our Strengths

We believe that our company and AV-101 possess the following attributes that increase the likelihood that we will be successful in developing and commercializing AV-101:

- **Significant efficacy of oral imatinib**. In the global Phase 3 IMPRES trial, oral imatinib demonstrated statistically and clinically significant efficacy following 24 weeks of treatment on top of PAH standard of care. These results were notable for achieving statistically significant improvements in the study's primary efficacy endpoint, 6MWD, and a key secondary endpoint, PVR, but also for hitting statistical significance on other clinically relevant efficacy endpoints on top of standard of care, which included at least two background PAH therapies. The primary endpoint of the Phase 2b portion of our Phase 2b/3 trial is the change in PVR following 24 weeks of treatment. The primary endpoint of the Phase 3 portion of our Phase 2b/3 trial is the change in 6MWD following 24 weeks of treatment. Our Phase 2b/3 trial is designed to treat a similar patient population to the IMPRES trial, patients in WHO Functional Classes II-IV taking at least two background PAH therapies.
- **Distinct PAH treatment mechanism**. Unlike all approved treatments for PAH, which act primarily through vasodilation, AV-101 is designed to directly address the abnormal cellular proliferation in the pulmonary vasculature that causes the increased resistance to blood flow and heart failure. We believe AV-101's mechanism uniquely positions our product candidate, if approved, for combination therapy with existing vasodilator treatments.
- **Adaptive development path**. We have planned an innovative Phase 2b/3 clinical trial based on an adaptive design that could lead to a potential NDA filing. Our development plan also benefits from our ability to leverage prior toxicology work done with oral imatinib.
- **Improved tolerability based on route of administration**. Our inhaled administration is designed to minimize systemic exposure and limit the safety and tolerability concerns observed in the IMPRES trial of oral imatinib in PAH. Our Phase 1 results in healthy volunteers demonstrated that plasma levels of imatinib were lower than those observed with the 400 mg oral dose of imatinib used in the IMPRES trial.
- **Expected comparability of concentrations of drug delivered**. Based on the results of our Phase 1 trial and our modeling, we expect lung concentrations of imatinib delivered by AV-101 in the 35 mg and 70 mg doses, both BID, selected for the Phase 2b portion of our Phase 2b/3 trial to overlap or surpass the lung concentrations predicted with the 400 mg oral dose in our Phase 1 trial, which was the same target dose used in the Phase 3 IMPRES trial.
- **Powerful barriers to entry**. We have generated strong intellectual property claims and other barriers to entry. We have filed for protection of our proprietary imatinib formulation, our drug product and methods of use. In addition, we have obtained exclusive access to a commercially available dry powder delivery device which we believe will create a substantial competitive advantage.
- **Substantial and readily addressable market opportunity.** If AV-101 is approved, we believe there is a substantial medical need and market opportunity for combining AV-101 with existing standard of care, which is often two or three background agents. Beyond this base case, we also believe that AV-101, if approved, could benefit a larger group of PAH patients with earlier-stage disease such as those patients receiving only one other PAH therapy.
- **Strong leadership in PAH**. Our executive management team has extensive experience in the clinical development of treatments for PAH, including Dr. Gillies who has been developing drugs for PAH for more than 20 years and most recently ran the AMBITION trial that established the current first-line PAH combination therapy and Dr. Niven's experience manufacturing development for inhaled small molecules. In addition, our Clinical Advisory Board includes several of the premier thought leaders in PAH who have extensive experience developing drugs and caring for patients suffering from PAH.

Our Strategy

Our strategy is to develop and commercialize AV-101 for patients suffering from PAH. Key elements of our strategy include our plans to:

- **Complete regulatory discussions for AV-101 in the United States and Europe**. At our April 14, 2021 end-of-Phase 1 meeting with the FDA, we received regulatory guidance that our Phase 2b/3 trial could support a NDA submission using the change in 6MWD compared to placebo as the primary endpoint

in the Phase 3 portion of the trial; however, the process of clinical development is inherently uncertain and there can be no guarantee that we will obtain marketing approval. We have been granted orphan designation for PAH from the FDA. We completed the formal process of seeking scientific advice and regulatory guidance from the European Medicines Agency, or EMA, regarding its requirements for regulatory approval and we believe that, if successful, our existing clinical program could support a marketing authorization application, or MAA submission for regulatory approval in Europe. We have received a positive opinion for orphan drug designation from the EMA's Committee for Orphan Medicinal Products in the European Union.

- **Advance AV-101 through NDA submission**. We plan to commence patient enrollment in a Phase 2b/3 trial of AV-101 in PAH in the second half of 2021. The Phase 2b portion of this trial will be a dose-ranging trial in which PVR will be the primary endpoint. The Phase 3 portion of the trial will be based on the optimal dose selected in the Phase 2b portion. 6MWD will be the primary endpoint.
- **Commercialize AV-101 directly in the United States**. If AV-101 is approved by the FDA, we intend to commercialize it ourselves in the United States with a specialty sales force focused primarily on pulmonologists and cardiologists treating adult patients suffering from PAH. We will consider entering into collaborations for the development and commercialization of AV-101 in Europe, Asia or other geographic regions, if approved by foreign regulatory authorities.
- **Pursue additional indications for AV-101**. We believe that AV-101 could have clinical applications in other groups of PAH patients, such as those with earlier-stage disease who may be receiving only one other PAH therapy. We also may consider the potential use of AV-101 in other types of pulmonary vascular disease.
- **Expand our pipeline by accessing additional product opportunities**. We plan to search for additional product opportunities available for license or acquisition that could be supported by the commercial infrastructure we build to successfully launch AV-101 in the United States if it is approved for marketing.

PAH Background and Limitations of Current Treatments

PAH is a progressive, life-threatening orphan disease characterized by increased pressure in the pulmonary arteries, vessels responsible for carrying deoxygenated blood from the heart to the lungs. This increased pressure is caused by narrowing of these blood vessels as a result of dysregulation of cells of the arterial wall, leading to excessive growth and proliferation. Over time, blood flow worsens as inflammatory cells are recruited and inflammatory cytokines further stimulate the proliferation of blood vessel cells. This ultimately leads to tissue scarring, fibrosis and blood vessel remodeling, resulting in severe restriction of blood flow (as illustrated in the figure below) and increased risk of developing blood clots and heart failure.

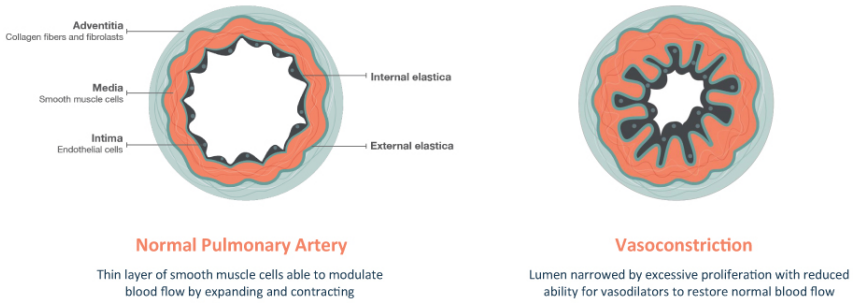

Figure 1. Increased pulmonary resistance is caused by cell proliferation that obstructs blood flow.

This severe restriction of blood flow also causes the heart to work harder to circulate blood through the lungs causing abnormal strain on the right ventricle of the heart. This restriction of blood flow and abnormal strain on the right ventricle results in PAH symptoms that worsen over time; these commonly include breathlessness, fatigue, chest pain, fainting or light headedness, as well as abdominal distension.

Four PAH functional classes categorize patient symptom severity and ability to carry out physical activity. Higher numbered functional classes indicate worsening symptoms and are associated with higher mortality. The four functional classes established by the World Health Organization, or WHO, are detailed in the figure below.

FIGURE 2. WHO PAH FUNCTIONAL CLASSES

FUNCTIONAL CLASS	DESCRIPTION
I	No limitation of physical activity, and ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
II	Slight limitation of physical activity, but patients are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
III	Marked limitation of physical activity, but patients are still comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain or near syncope.
IV	Patients are unable to carry out any physical activity without symptoms, and discomfort is increased by any physical activity. Signs of right heart failure manifest, and dyspnea and/or fatigue may even be present at rest.

Prevalence of PAH and Unmet Need

Based on third-party estimates, the number of PAH patients diagnosed is between 30,000 and 40,000 in the United States with an average age at diagnosis of 53 years old and 65% to 80% of those diagnosed being women. The exact prevalence of PAH worldwide is not known but it has been estimated to be between 10 to 52 cases per million. Many drugs have been developed and made commercially available for the treatment of PAH, such as vasodilators, and it is estimated that the combined global sales for PAH products in 2020 was $5.4 billion. While advances in the treatment of PAH using vasodilatory agents over the last two decades have markedly improved median survival, PAH patients still face significant disease burden and premature death. The five-year survival rate for newly diagnosed and prevalent patients is between 61% and 65%. Clearly there is unmet need for new therapies beyond the standard of care.

Limitations of Current Therapies for PAH

The current standard of care in PAH consists of drugs that act primarily as pulmonary vasodilators, which relax the muscles in the pulmonary arterial walls, thereby reducing the degree of blood vessel constriction. Although the current standard of care provides some benefit to patients, it is clear from the pathology of PAH that abnormal cellular proliferation causes progressive narrowing of the pulmonary vasculature. This abnormal proliferation is not addressed by therapies currently used to treat PAH.

Three classes of pulmonary vasodilators are currently used to treat PAH: endothelin receptor antagonists, nitric oxide pathway modulators and prostacyclins.

- **Endothelin Receptor Antagonists**. Some treatments currently approved for PAH work by blocking the action of endothelin-1, a potent vasoconstrictor, and are referred to as endothelin receptor antagonists, or ERAs. These drugs include bosentan, macitentan and ambrisentan. All three of these drugs are orally administered and improve blood flow to the lungs as determined by measures of hemodynamics such as pulmonary vascular resistance and cardiac output, which translates to improvements in exercisability as measured by the distance that patients can walk in a fixed period of time (6MWD).
- **Nitric oxide pathway modulators such as PDE5 inhibitors and sGC's**. Nitric oxide is a naturally occurring molecule that is widely recognized as important in a number of biological processes. It causes blood vessels to relax and widen via the second messenger cGMP, resulting in an increase in blood flow. Two common modalities utilize the nitric oxide pathway to result in vasodilation: Phosphodiesterase type 5, or PDE5, inhibitors prevent the breakdown of cGMP and soluble guanylate cyclase stimulators, or sGC's, increase the production of cGMP independent of nitric oxide. Several oral PDE5 drugs are available, such as sildenafil and tadalafil. Additionally, riociguat is the only sGC approved for PAH.
- **Prostacyclin pathway modulators**. Patients with PAH have been shown to have reduced levels of prostacyclin, a naturally occurring lipid that has the effect of relaxing the smooth muscles surrounding

arteries, resulting in vasodilation. Prostacyclin analogues, such as iloprost and treprostinil, are approved therapies for PAH. Selexipag is an oral prostacyclin-like drug approved for PAH. In addition to the challenges associated with dosing, prostacyclin therapy can be difficult to tolerate. In clinical trials subcutaneous infusion of these agents has shown severe infusion site adverse events requiring narcotics for these symptoms. The oral prostacyclins also have a high incidence of headache and diarrhea, nausea, vomiting, and flushing, which can lead to discontinuations.

PAH patients are often treated with more than one of these drugs and new therapies are typically added to existing therapies rather than replacing drugs that are providing insufficient benefit. Based on third party sources, we estimate that approximately 50% of patients are taking two or three FDA approved drugs for the treatment of PAH. Oral therapies are commonly prescribed first-line, typically consisting of an ERA and PDE5 inhibitor. As patients progress in their disease severity, a prostacyclin can typically be added as a third agent. Although these therapies have been shown to improve exercise capacity, quality of life, pulmonary pressure and short-term survival, none of the current treatments are curative and patients remain on life-long therapy with poor long-term prognosis.

Our Approach, AV-101

We are developing AV-101 as a drug/device combination product that delivers imatinib directly to the lungs via inhalation. The product consists of capsules of particulate imatinib that will be used in conjunction with a dry powder inhaler device. We believe that delivery of imatinib directly to the lungs will maximize the amount of drug in the targeted tissues while minimizing systemic exposure. Furthermore, we believe that delivering imatinib in this way may improve the tolerability of treatment while maintaining imatinib's known effects on exercise capacity and hemodynamics. AV-101 has been granted orphan drug designation by the FDA for the treatment of PAH.

Potential of Imatinib to Treat PAH

The molecule in AV-101, imatinib, has demonstrated improvement on the primary and multiple secondary endpoints in a global Phase 3 trial (IMPRES) conducted by Novartis in PAH patients on top of at least two standard of care PAH drugs. However, when administered orally, serious adverse events, and discontinuations were high and the oral version was never approved for PAH. We believe imatinib is unique amongst tyrosine kinase inhibitors for its specificity and potency. At pharmacologically achievable levels, it inhibits only a handful of kinases, such as PDGFR, KIT, DDR and ABL, which have been implicated in PAH disease processes. Recent academic focus on kinase inhibition in PAH has been on PDGFR. However, other kinase inhibitors that hit PDGFR also inhibit the closely related SRC and VEGFR kinases, inhibition of which have caused or exacerbated PAH. Thus we believe clinical success in PAH is not dictated by inhibiting PDGFR alone, but rather the kinase inhibition profile and targeted delivery of the molecule to the lungs. We are encouraged that imatinib, the molecule in AV-101, has shown clinical effects in the IMPRES trial, and we believe inhaled delivery of AV-101 limits systemic exposure and may mitigate the tolerability issues observed with oral imatinib.

Kinase inhibitors have been approved for the treatment of various cancers. Case reports of improvements in PAH in patients receiving oral imatinib, marketed as Gleevec by Novartis, led to several clinical trials designed to test the efficacy of imatinib for PAH. The IMPRES trial was a randomized, double-blind global Phase 3 trial conducted by Novartis that enrolled 202 PAH patients. Most of these patients had Functional Class II or Class III PAH and were already on at least two background therapies. Patients were randomized to receive oral imatinib or placebo for 24 weeks.

Patients enrolled in the IMPRES trial had reduced exercise capacity compared to healthy adults as measured by the six-minute walk distance, or 6MWD, a simple test that has been used as a primary endpoint for the approval of multiple drugs to treat PAH. The mean baseline 6MWD for patients in this trial was 361 meters, whereas for healthy adults it has been reported to be approximately 600 meters The baseline 6MWD values in these patients upon enrollment was below normal for healthy adults despite the fact that they were all on treatment with at least two PAH therapies and 41% were on triple therapy, the maximal standard of care for PAH. Patients remained on their respective pre-trial PAH therapies throughout the trial.

The target dose of oral imatinib in the IMPRES trial was 400 mg/day which is an approved dose of oral imatinib for the treatment of cancers such as chronic myelogenous leukemia, or CML, and metastatic malignant gastrointestinal stromal tumors, or GIST, containing specific genetic alterations. Treatment of PAH patients with 400 mg oral imatinib led to a significant improvement in 6MWD over baseline compared to placebo. This

difference became significant at 12 weeks and continued to separate from placebo until the end of the trial at 24 weeks, at which point the oral imatinib-treated patients achieved an average improvement of 32 meters in the 6MWD (p=0.002). The magnitude of this improvement is notable because no other PAH drug has shown such an improvement in a Phase 3 trial on top of at least two background therapies. The most recently approved oral PAH drug, Uptravi (Selexipag), showed a 12-meter treatment effect in the Phase 3 GRIPHON trial. The patients in this trial were not as heavily treated as those in the IMPRES trial, with one third on double therapy and none on triple therapy. The figure below shows the improvement over time in 6MWD of PAH patients treated with oral imatinib on at least two standard of care therapies as compared to the placebo group in the Phase 3 IMPRES trial.

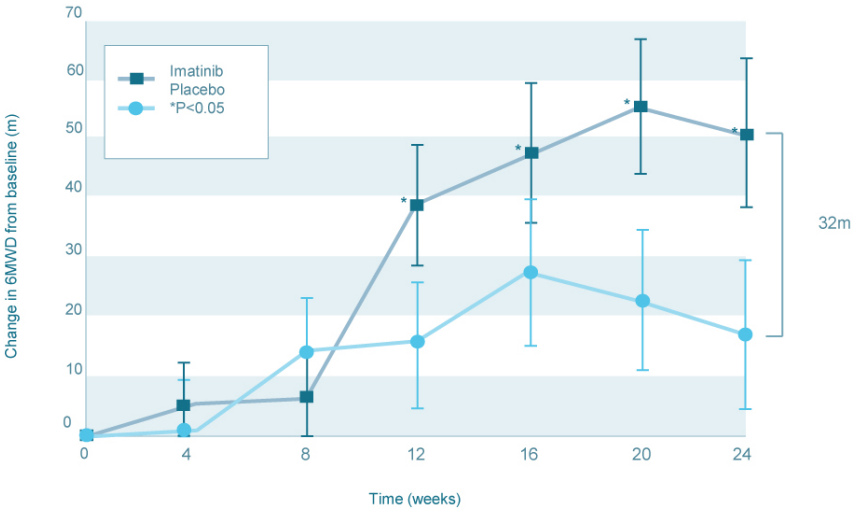

Figure 3. Imatinib led to a significant increase in 6MWD on top of at least two standard of care therapies

The improvement in 6MWD with oral imatinib treatment was observed across all patient subgroups regardless of treatment with other PAH therapies (as seen in the figure below). We believe this observation suggests that oral imatinib improved 6MWD through a mechanism that was independent of patients' background therapies.

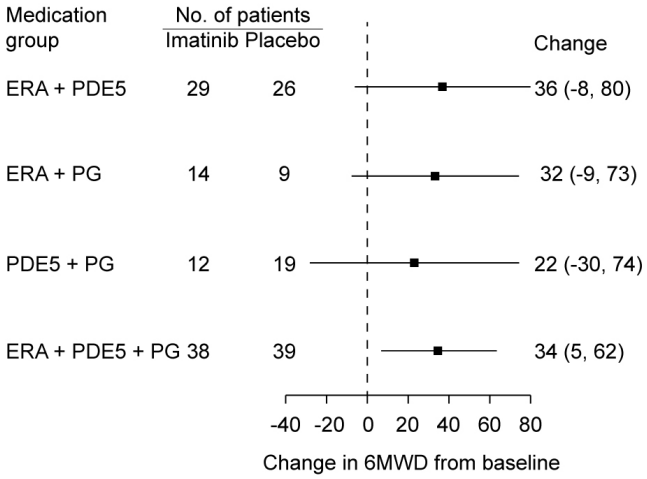

Figure 4. Imatinib led to improvements in 6MWD compared to placebo regardless of patients being treated concurrently with at least two approved PAH therapies

In addition to improvements in 6MWD, patients treated with imatinib had greater improvements in multiple secondary endpoints, including measures of hemodynamics. Importantly, there was a significant improvement at 24 weeks in PVR ($p<0.001$), a measure of how difficult it is for blood to circulate through the lungs. Damaged pulmonary blood vessels make it more difficult for the heart to pump blood through the lungs, leading to increased pulmonary arterial pressure, increased workload on the heart, and if not resolved, heart failure. PVR is frequently used as a quantitative measure in PAH Phase 2 trials to determine the appropriate dose for registrational Phase 3 trials that directly measure changes in patient exercise capacity, such as 6MWD. Patients treated with imatinib had a significant reduction in PVR at 24 weeks, as noted in the blue box in the figure below. PVR was virtually unchanged compared to baseline in placebo treated patients. Consistent with the improvements in PVR, significant improvements compared to placebo treated patients, as shown in the figure below, were also observed in mean pulmonary artery pressure, or mPAP, which was decreased by 5.2 mm Hg; cardiac output, or CO, which was increased by 0.88 liter/min; and right arterial pressure, or RAP, which was decreased by 1.7 mm Hg. An echcardiography sub-study of 74 IMPRES patients showed that patients randomized to oral imatinib showed significant improvements in certain measures of right ventricle function after 24 weeks compared with placebo. Significant and consistent changes across hemodynamic and echo measures suggest a benefit of imatinib for the treatment of PAH with the potential to result in long-term improvements in pulmonary and cardiac function.

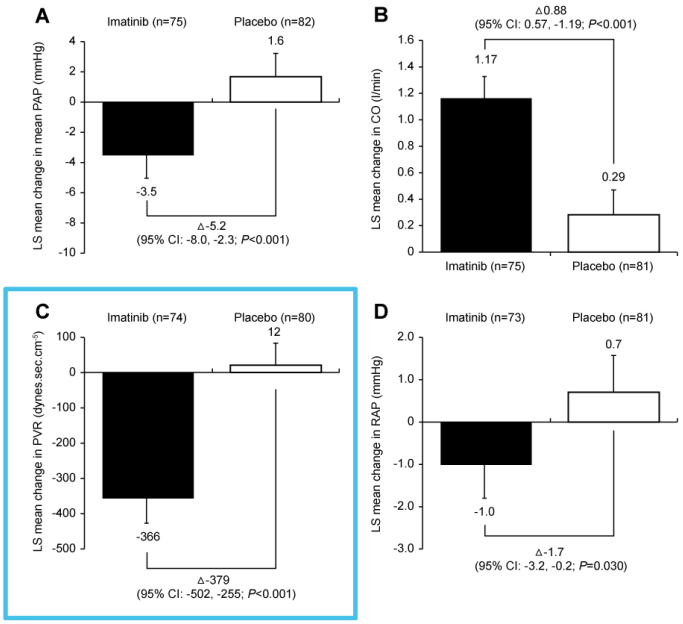

Figure 5. Imatinib treatment led to significant improvements across multiple secondary endpoints including PVR (highlighted), an endpoint frequently used in Phase 2 dose-finding trials[1]

(1) Patients included in analyses of hemodynamic parameters include those who completed the study plus those who discontinued early but had a right heart catheterization performed at discontinuation.

Long-Term Extension Study

Patients who completed the 24 week trial were eligible to be enrolled in an open label long-term extension study. The improvements in 6MWD achieved at 24 weeks were sustained during this extension and the mean difference in 6MWD compared to baseline improved up to 144 weeks in patients that were able to tolerate the treatment. Although these results were very encouraging, data from the extension trial also highlighted the major limitation in using oral imatinib to treat PAH, which was drug tolerability. Of the 103 patients originally randomized to the imatinib arm of the core trial, only 21 remained on therapy after 180 weeks of dosing. The patients who were able to tolerate the drug long term showed a durable continued improvement in 6MWD.

Safety and Tolerability

The relatively poor tolerability of oral imatinib poses challenges for the potential use in PAH patients. The AEs observed in the IMPRES trial were consistent with the AE profile observed in cancer trials, with the exception of subdural hematoma (which was only observed in the IMPRES trial), and led to a significant number of discontinuations, which limited oral imatinib's potential as a therapy for PAH. Specifically, 44% of patients treated with oral imatinib in the IMPRES trial experienced fluid retention, which is of particular concern in PAH patients who commonly experience heart failure. The figure below lists the AEs reported in the 24-week Phase 3 IMPRES trial of oral imatinib in PAH patients on two or more standard-of-care therapies.

	Imatinib n=103 (%)	Placebo n=98 (%)
Adverse Event	100 (97)	94 (96)
Nausea	57 (55)	23 (24)
Peripheral edema	45 (44)	20 (20)
Diarrhea	36 (35)	19 (19)
Vomiting	31 (30)	10 (10)
Periorbital edema	30 (29)	7 (7)
Headache	25 (24)	22 (22)
Dyspnea	19 (18)	13 (13)
Nasopharyngitis	18 (18)	19 (19)
Hypokalemia	16 (16)	3 (3)
Anemia	14 (14)	3 (3)
Cough	11 (11)	15 (15)
Fatigue	11 (11)	7 (7)
Face edema	10 (10)	1 (1)
Muscle spasms	10 (10)	2 (2)

Figure 6. Adverse events reported in >10% of the Imatinib group in the 24-week IMPRES trial, not including the trial extension

In the IMPRES trial, there were 45 serious adverse events reported in imatinib treated patients, including some that were of particular concern for PAH patients, who already have compromised cardiac function. These included worsening of PAH; anemia; dyspnea, or shortness of breath; peripheral edema; and presyncope, or lightheadedness. Of note, subdural hematoma occurred in eight patients (two in the core study (1.9%), six in the trial extension (4.2%)) receiving imatinib and anticoagulation.

	Imatinib n=103 (%)	Placebo n=98 (%)
Serious Adverse Event	45 (44)	29 (30)
Worsening of pulmonary hypertension	6 (6)	8 (8)
Anemia	7 (7)	1 (1)
Dyspnea	6 (6)	2 (2)
Peripheral edema	6 (6)	0
Presyncope	5 (5)	0
Diarrhea	3 (3)	2 (2)
Device-related infection	3 (3)	0
Syncope	1 (1)	5 (5)
Subdural hematoma *	2 (2)	0

Figure 7. Serious adverse events reported in the IMPRES 24-week trial publication, not including the trial extension

Patients enrolled in the IMPRES trial that were not able to tolerate 400 mg/day of imatinib did not see a significant improvement in 6MWD after 24 weeks. As shown in the figure below, those patients who were not dosed with 400 mg/day for more than half of the time did not achieve the improvements in 6MWD that were significantly distinguished from those achieved by placebo treated patients. These results suggest that addressing the adverse events and tolerability of imatinib in PAH patients cannot be achieved by lowering the oral dose without sacrificing this improvement. Further development of oral imatinib for the treatment of PAH was discontinued by Novartis.

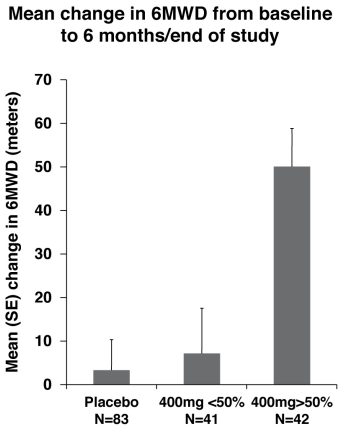

Figure 8. Patients who were dosed with 400 mg/day for less than half of the duration of the trial did not achieve a significant improvement in 6MWD

AV-101, an inhaled formulation of imatinib

AV-101 is designed to deliver imatinib directly to the lungs to maximize the amount of drug in the targeted tissues while minimizing systemic exposure. We believe that delivering imatinib in this way may maintain imatinib's potential therapeutic benefits while improving the tolerability of treatment. The oral version of imatinib, marketed as Gleevec, is delivered as tablets containing imatinib mesylate which is a salt of imatinib. Imatinib mesylate is not readily amenable to being used in an inhaled formulation because it absorbs water from the atmosphere if not stored in a rigorously controlled environment. Moisture uptake would lead to potential stability concerns and a high likelihood of poor delivery performance when inhaled from any dry powder inhaler device. We also believe mesylate salt would be a poor choice for an inhaled PAH therapy for additional reasons: (i) the mesylate group introduces a genotoxic risk; (ii) it increases the formulation risk due to the existence of multiple crystal forms; and (iii) delivery using the mesylate salt has the potential to release the acidic mesylate upon deposition on the lung surface which could lead to transient irritation and increase the propensity for cough. We therefore explored other salt and polymorphs of imatinib to identify a more suitable formulation for an inhaled therapy without altering the active molecule. We discovered a form that exhibited what we believe to be almost ideal physical chemical properties for development as a dry powder for inhalation using capsules in a simple dry powder inhaler, or DPI.

We also believe that dry powder inhalation is the most convenient mode of delivery to the lungs for patients. The prospective advantages of dry powder inhalation include that such formulations (i) can be delivered via a convenient, portable and easy-to-use delivery system; (ii) avoid the cords or batteries or bulky equipment that may be needed with nebulizers; (iii) carry less risk of microbial contamination due to the low moisture content powder; (iv) have better anticipated shelf stability of the drug product compared to a solution dosage form; and (v) can potentially improve lung retention of the powder imatinib compared to an aqueous nebulizer formulation, which may result in reduced dose, dose frequency and peak exposure in the circulation.

AV-101 Phase 1

We have completed a placebo-controlled, randomized, double-blinded, single ascending dose and multiple ascending dose Phase 1 trial of AV-101 in 82 healthy volunteers. Doses tested in the single ascending dose, or SAD, portion ranged from 1 to 90 mg of AV-101. A 400 mg dose of oral imatinib was included as a comparator. The multiple ascending dose, or MAD, portion tested 10 mg, 30 mg and 90 mg BID for seven days. The purpose of the trial was to establish safety and tolerability of AV-101 and to demonstrate that systemic levels of AV-101 were lower than oral imatinib.

All doses resulted in lower systemic plasma levels of imatinib compared to those observed following a single 400 mg oral dose. In the figure below, the blue dashed line shows simulated steady state levels of oral imatinib in the blood extrapolated from the 400 mg cohort in the SAD potion of our Phase 1 trial. These levels are consistent with multiple publications on oral imatinib pharmacokinetics. The other lines show the blood concentrations following the final dose of AV-101 in the MAD portion of our Phase 1 trial, on day 7, when steady state concentrations had been achieved. The dotted part of the 90 mg dose shows a simulated representation of an additional dose twelve hours later to illustrate steady state BID dosing.

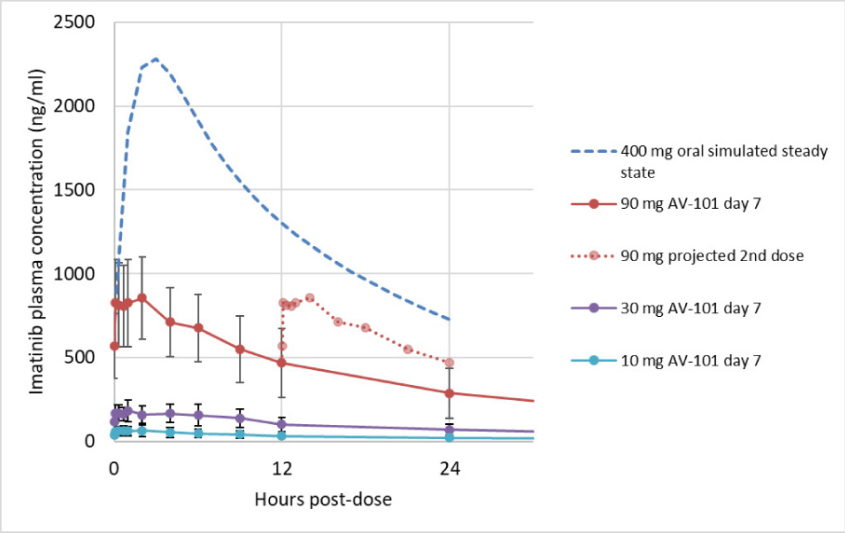

Figure 9. Phase 1 systemic exposure of AV-101 vs 400 mg oral imatinib.

We also predicted lung exposures using a physiologically based pharmacokinetic, or PBPK, model built from a published method to extrapolate lung exposures from blood levels, which was informed by our Phase 1 plasma data. Although there is inherent uncertainty associated with all models that extrapolate data, we expect the exposures of imatinib obtained in the lungs at the dose range we intend to use in the Phase 2b portion of our Phase 2b/3 trial of 10 mg, 35 mg and 70 mg, all BID, to overlap or surpass lung levels predicted from 400 mg oral imatinib. The dashed blue line in Figure 11 shows lung exposures extrapolated from published steady state PK data and informed by our Phase 1 plasma data for oral imatinib at 400 mg. The solid lines show extrapolated lung levels of AV-101 doses using our PBPK model.

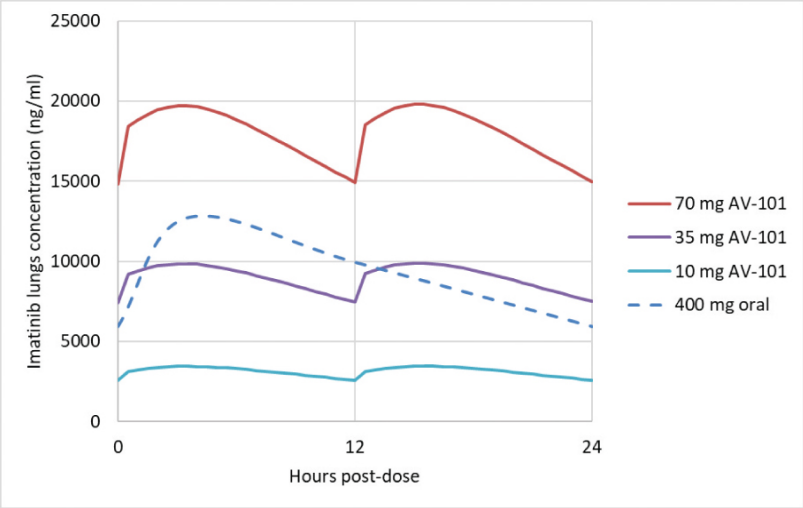

Figure 10. Predicted Phase 2b lung exposures from dosing of 10, 35 and 70 mg AV-101. We expect the lung exposures of imatinib delivered by AV-101 in the dose range to overlap or surpass the predicted lung exposures from 400 mg oral imatinib

Safety and Tolerability in Phase 1 trial

There were no serious adverse events reported in our Phase 1 trial. There were no changes in vital signs including pulmonary function testing and oxygen saturations. Of the less severe adverse events, there was one discontinuation at the highest dose due to vomiting and the most frequent adverse event was a cough that was reported in 55% of volunteers at the highest 90 mg dose. This cough was transient, predominantly mild in nature, resolved on its own within 30 minutes and did not lead to any discontinuations. We believe that the cough may be a function of the total amount of powder delivered in the high Phase 1 dose. The intended dosing for the Phase 2b/3 trial will use less than 40% of the amount of powder that was inhaled at the highest Phase 1 dose. The figure below shows the adverse events reported in our Phase 1 MAD trial of AV-101 in healthy volunteers.

Adverse Event n(%)	10 mg (n=8)	30 mg (n=9)	90 mg (n=9)
Cough	1 (13)	1 (11)	5 (56)
Persistent cough	-	-	-
Headache	-	-	4 (44)
Nausea	-	-	2 (22)
Chest discomfort	-	-	2 (22)
Throat irritation	-	1 (11)	1 (11)
Musculoskeletal pain	-	-	2 (22)

Single incidence AEs: Vomiting (discontinued), Dysgeusia, Musculoskeletal chest pain, Nasal congestion, Oropharyngeal pain, Back pain, Abdominal pain, COVID-19, Presyncope, Alanine aminotransferase increased

Figure 11. Adverse events reported in the Phase 1 MAD trial of AV-101 in healthy volunteers

We submitted to the FDA summaries of the safety and tolerability findings from our Phase 1 trial along with the systemic plasma levels for the participants from the trial. We also submitted information on our drug substance and drug product. At our April 2021 meeting, we reached alignment with the FDA that our Phase 2b/3 trial design was acceptable and could, if successful with strong results, support a NDA submission using the change in 6MWD compared to placebo over 24 weeks as the primary endpoint in the Phase 3 portion of our trial.

AV-101 Phase 2b/3 trial

In the second half of 2021, we intend to initiate a trial in Functional Class II through Class IV PAH patients with inadequate disease control on at least two approved PAH therapies. We are designing this trial as a global, Phase 2b/3 trial. This clinical trial will establish the target dose in the Phase 2b portion then expand into a Phase 3 efficacy trial using the selected dose. The Phase 2b portion of this double-blind, placebo-controlled randomized trial is designed to assess safety and tolerability using change in PVR, an objective measure of the effect of AV-101 on hemodynamic function in PAH patients, as the primary endpoint to inform the selection of the appropriate dose for the Phase 3 portion of the trial. Change in 6MWD compared to placebo will be a secondary endpoint, and all efficacy endpoints will be measured following 24 weeks of treatment. The Phase 3 portion of the trial will use the change in 6MWD compared to placebo at 24 weeks as the primary endpoint. Secondary endpoints in the Phase 2b/3 trial will include N-terminal pro B-type natriuretic peptide, or NT-proBNP, a biomarker associated with heart failure; hemodynamic parameters; clinical worsening; clinical improvement; change in functional class; change in risk score; and quality of life measures. All patients completing the Phase 2b or Phase 3 portions will be invited to enter a long-term extension trial of AV-101.

Phase 2b/3 Enrollment and Timing

The Phase 2b/3 trial will be a single continuous trial made up of three periods.

- Period 1 will be the Phase 2b enrollment portion of the trial. Approximately 200 patients will be enrolled across four treatment arms, which include three dose groups of AV-101 and one placebo group. The primary endpoint is the change in PVR compared to placebo at 24 weeks. Data from the Phase 2b portion will inform the selection of an optimal dose of AV-101 for Phase 3. We anticipate that topline Phase 2b data will be available in the middle of 2023.

- Period 2 begins as soon as enrollment completes in the Phase 2b portion of the trial. This second period signifies the start of enrollment in the Phase 3 portion of the trial. We expect to complete enrollment of the Phase 2b portion of the trial by the end of 2022 and commence enrollment of the Phase 3 portion thereafter.
- Period 3 begins once the optimal dose is selected and will then only enroll across two treatment arms, the optimal dose of AV-101 and the placebo arm. Once the final patient enrolled has completed 24 weeks on study, the Phase 3 portion of the trial is complete.

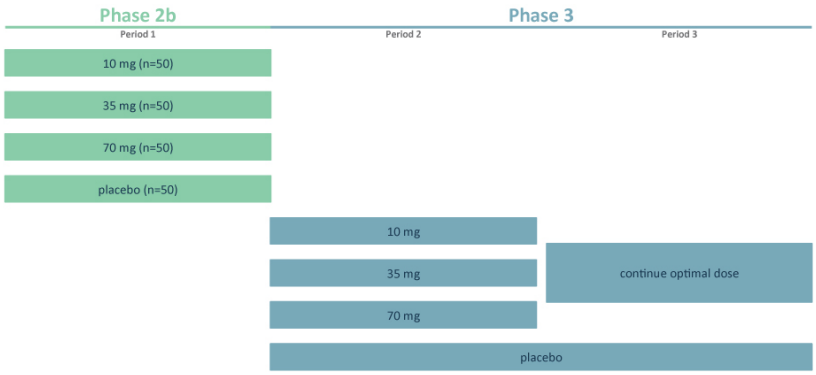

Figure 12. Design of the Phase 2b/3 trial of AV-101 in PAH patients

If the results of the Phase 3 portion of this trial show a statistically significant and potentially clinically meaningful benefit in 6MWD, we plan to submit a NDA, with the FDA for AV-101 for the treatment of PAH.

Confirmation of the Potential of Antiproliferative Medicines as a Novel Class of PAH Therapeutics

Although no approved PAH therapy directly addresses the underlying cell proliferation that leads to increased pulmonary arterial pressure, the concept behind targeting cell proliferation to treat PAH is not new. The most advanced antiproliferative compound in the clinic is sotatercept, a molecule that blocks signaling of members of the TGF-beta family of growth factors. Results from a Phase 2 clinical trial in PAH showed that sotatercept led to a reduction in PVR, providing further support for the therapeutic potential of antiproliferative product candidates in PAH. We are encouraged by these results as they provide independent confirmation of the importance of antiproliferative products as a potentially broad class of PAH therapeutics to complement vasodilators. Similar to the vasodilator field, we believe that PAH patients may benefit from treatment with multiple antiproliferative therapies directed against different targets.

Manufacturing and Supply

We use third-party contract manufacturers for the production of AV-101. Our active pharmaceutical ingredient, or API, is produced at two contract manufacturers. The starting material for our API is manufactured and in compliance with the FDA's current Good Manufacturing Practice, or current GMP, regulations and European Pharmacopoeia, or EP, standards. The final step in the manufacture of API is completed in Spain at Uquifa S.A., or Uquifa, which is required to comply with the FDA's current GMP regulations. AV-101 finished product is processed for aerosol use and filled into capsules by our contract fill/finish provider in the United States at a division of Lonza Group Ltd, or Lonza, which is required to comply with current GMP regulations. As AV-101 is a drug-device combination product, we expect to contract with a third-party to manufacture the single-dose inhaler device that we plan to use for delivering inhaled AV-101 to patients in our Phase 2b/3 clinical trial.

We currently plan to manufacture API at Lonza and Uquifa for our future clinical trials. Release and stability testing for API and finished product are performed at Lonza. The testing to date shows stability of at least 18 months for one batch of API under conditions at a temperature of 25^{o} Celsius and 60% relative humidity and 12 months for our bulk aerosol. We expect that stability testing for our API to reach at least 24 months and stability for our drug product to reach 18 months at the time we see topline data from our Phase 2b/3 clinical trial.

At our April 2021 meeting, the FDA confirmed that our API, finished product, and single-dose inhaler producers are acceptable for a Phase 2b/3 clinical trial. We are in the process of having finished product manufactured for the Phase 2b/3 clinical trial and expect the finished product material packaged with the single-dose inhaler to be ready for shipping to clinical sites in August 2021, and prior to the start of patient enrollment.

In anticipation of a potential NDA filing, we plan to manufacture a minimum of three batches of API, finished product, and single-dose inhaler devices for registration purposes and to test these batches for stability with a goal of establishing a commercial shelf life of at least two years for finished product and a longer expiry for API.

Sales and Marketing

Our commercialization strategy is to develop AV-101 into a leading therapy worldwide for the treatment of PAH.

Our Chief Executive Officer has significant commercial experience, but we have not yet established a sales and marketing organization. We intend to recruit our own specialty sales force in the United States focused on promoting AV-101. We plan to target our marketing and sales efforts to pulmonologists and cardiologists who specialize in treating PAH. We believe a specialty sales force of approximately 75-100 representatives, supported by reimbursement specialists and a medical affairs team, will enable us to call on the pulmonologists and cardiologists who specialize in treating PAH.

We believe that the market for AV-101 in the five largest countries in the European Union represents the bulk of the potential European market and that China and Japan represent the bulk of the potential Asian market. We plan to enter one or multiple collaborations to commercialize AV-101 in Europe and Asia.

We believe AV-101 will be reimbursed appropriately by public and commercial payors.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our products, novel discoveries, drug development technologies and know-how; to operate without infringing on or otherwise violating the proprietary rights of others; and to prevent others from infringing or otherwise violating our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing or in-licensing U.S. and foreign patents and patent applications related to our products and other proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trademarks, trade secrets, know-how, continuing technological innovation and potential in-licensing opportunities to develop and maintain our proprietary position.

Our intellectual property portfolio includes pending patent applications in the United States and under the Patent Cooperation Treaty (PCT international applications). The PCT international applications preserve all of our rights to file patent applications in commercially relevant foreign jurisdictions for our products. As of June 22, 2021, we own nineteen U.S. patent applications (eight of which are U.S. nonprovisional applications and eleven of which are U.S. provisional applications), and two pending PCT international applications. Our U.S. patent portfolio is expected to expire between May 14, 2040 and February 15, 2042, excluding any extension of patent term that may be available and assuming that the filed patent applications will issue as patents. Our foreign patent portfolio is expected to expire between May 14, 2040 and February 15, 2042, excluding any extension of patent terms that may be available and assuming that filed applications will issue as patents and that the foreign patent terms are calculated similarly to the calculation of U.S. patent terms for the corresponding U.S. portion of the patent portfolio. Our pending patent applications are summarized in the following table.

APPLICATION NO.	RELATED PRODUCT	PROTECTION SOUGHT	PROJECTED EXPIRATION*	JURISDICTION
62/849,054	AV-101	Composition of Matter; Use	N/A	US
16/874,111	AV-101	Composition of Matter; Use	5/14/2040	US
PCT/US20/32872	AV-101	Composition of Matter; Use; Process	N/A	International PCT
62/849,056	AV-101	Composition of Matter; Use	N/A	US
16/874,118	AV-101	Composition of Matter; Use	5/14/2040	US
62/849,058	AV-101	Process	N/A	US
16/874,122	AV-101	Process	5/14/2040	US
62/849,059	AV-101	Composition of Matter; Use	N/A	US
16/874,128	AV-101	Composition of Matter; Use	5/14/2040	US
62/877,575	AV-101	Composition of Matter; Process	N/A	US
16/874,143	AV-101	Composition of Matter; Process	5/14/2040	US
62/942,408	AV-101	Composition of Matter; Use	N/A	US
16/874,153	AV-101	Composition of Matter; Use	5/14/2040	US
62/984,037	AV-101	Use; Kit	N/A	US
16/874,168	AV-101	Use; Kit	5/14/2040	US
62/958,481	AV-101	Use	N/A	US
16/874,190	AV-101	Use	5/14/2040	US
PCT/US20/32874	AV-101	Use	N/A	International PCT
63/117,258	AV-101	Composition of Matter; Combination Products; Use	N/A	US
63/150,731	AV-101	Composition of Matter; Combination Products; Use	N/A	US
63/149,446	AV-101	Process; Composition of Matter	N/A	US

* Projected patent expiration dates were calculated for pending U.S. Nonprovisional Applications based on filing date. These calculations do not take into account any terminal disclaimers or patent term adjustments that may occur during prosecution. U.S. Provisional and International PCT filings will not issue as patents and therefore do not have a projected expiration date.

Our intellectual property estate strategy is designed to provide multiple layers of protection, including: (1) proprietary patent rights with claims directed to our drug product; (2) proprietary patent rights covering methods of treatment using our drug product; and (3) proprietary patent rights covering innovative manufacturing processes.

While we seek broad coverage under our pending patent applications, there is always a risk that a modification of the product or manufacturing process may allow a competitor to avoid infringement claims. In addition, patents, if granted, expire, and we cannot provide any assurance that any patents will be issued from our pending or any future applications or that any issued patents will adequately protect our products.

We have conducted freedom to operate, or FTO, analyses of the current patent landscape with respect to our lead product candidates. In doing so, we have strived to ensure our ability to operate freely within the complex patent landscape of inhalable kinase inhibitors and the use of such products in the field of PAH.

We are also working to develop new formulations of our drug products and new uses for such products, for which we intend to seek patent protection on our own to expand the layers of protection provided by our intellectual property estate.

Patent Protection and Terms

Individual patents extend 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, patents issued from regularly filed applications in the United States are granted a term of 20 years from the

earliest effective filing date. In addition, in certain instances, a patent term can be adjusted to recapture a portion of the United States Patent and Trademark Office, or the USPTO, delay in issuing the patent, and extended to recapture a portion of the patent term effectively lost as a result of the FDA regulatory review period of the drug covered by the patent. However, as to the FDA component, the restoration period cannot be longer than five years, the total patent term including the restoration period must not exceed 14 years following FDA approval of the drug, and the extension may only apply to one patent that covers the approved drug (and to only those patent claims covering the approved drug, a method for using it, or a method for manufacturing it). There can be no assurance that any such patent term adjustment or extension will be obtained. 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. However, the actual protection afforded by a patent varies on a product-by-product basis, from country to country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Furthermore, the patent positions of biotechnology and pharmaceutical products and processes like those we intend to develop and commercialize are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in such patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries can diminish our ability to protect our inventions and enforce our intellectual property rights, can make it easier to challenge the validity, enforceability or scope of any patents that may issue, and, more generally, could affect the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

Third-Party Patent Filings

Numerous U.S. and foreign issued patents and patent applications owned by third parties exist in the fields in which we are developing products. In addition, because patent applications can take many years to issue, there may be applications unknown to us, which may later result in issued patents that our products or proprietary technologies may infringe. Moreover, we may be aware of patent applications, but incorrectly predict the likelihood of those applications issuing with claims of relevance to us.

Under U.S. law, a person may be able to patent a discovery of a new way to use a previously known compound, even if such compound itself is patented, provided the newly discovered use is novel and non-obvious. Such a method-of-use patent, however, if valid, only protects the use of a claimed compound for the specified methods claimed in the patent. This type of patent does not prevent persons from using the compound for any previously known use of the compound. Further, this type of patent does not prevent persons from making and marketing the compound for an indication that is outside the scope of the patented method.

Trade Secrets and Other Protections

In addition to the protections afforded by patents and other regulatory protections, we may rely, in some circumstances, on trade secrets to protect our technology. Trade secrets may be useful to protect proprietary know-how that is not patentable or which we elect not to patent. Trade secrets may also be useful for processes or improvements for which patents are difficult to enforce.

We also protect our products and proprietary technology through confidentiality agreements with employees, consultants, advisors, contractors and collaborators. 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 through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any such breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our 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.

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Infringement of Third-Party Proprietary Rights

Our commercial success will depend in part on not infringing upon or otherwise violating the intellectual property and proprietary rights of third parties. If we are found to infringe a third party's intellectual property

rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could also be forced, including by court order, to cease commercializing the infringing product or technology. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our products or force us to cease some of our business operations. For more information regarding these risks, please see "Risk Factors—Risks Related to Our Intellectual Property."

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions.

Some of our potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors that will differentiate AV-101, if approved, are likely to be its efficacy, safety, convenience, price, and the availability of reimbursement from commercial, government and other third-party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We intend to seek approval for AV-101 initially for the treatment of PAH in patients taking two or more approved PAH therapies. We recognize that physicians have many treatment options for patients already taking two or more treatments for PAH, including prostanoids available in oral form as Orenitram (United Therapeutics Corporation, or United Therapeutics) and Uptravi (Janssen Pharmaceuticals, Inc., or Janssen), by inhalation as Tyvaso (United Therapeutics), and by infusion as Remodulin (United Therapeutics). We believe that AV-101, if approved, could be used prior to or in combination with prostanoids, and in combination with existing front-line agents such as the oral PDE5 inhibitors, including Revatio (Pfizer) and Adcirca (United Therapeutics); the sGC stimulator Adempas (Bayer AG); and oral ERAs, including Tracleer (Janssen), Letairis (Gilead) and Opsumit (Janssen). PAH is also an active indication for investigational drugs, and we may face competition in the future from sotatercept (Acceleron Pharma, Inc.), seralutinib (Gossamer Bio, Inc.), rodatristat (Altavant Sciences, Inc.) and/or PF-06842874 (Pfizer). To our knowledge, Tenax Therapeutics, Inc. and Aerami Therapeutics, Inc. have communicated interest in developing imatinib for PAH, and both companies are at a preclinical stage of development.

Government Regulation and Approval

United States—FDA Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The FDCA and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory authorities of the countries in which we wish to conduct studies or seek approval of our product candidates. Failure to comply with applicable United States requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs, withdrawal of an approval, warning or untitled letters, clinical holds, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, civil penalties, and criminal prosecution.

FDA approval is required before any new unapproved product or a product with certain changes to a previously approved product, including a new use of a previously approved drug, can be marketed in the United States. The steps required to be completed by the FDA before a drug may be marketed in the United States generally includes the following:

- completion of preclinical laboratory tests, animal studies, and formulation studies performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an investigational new drug, or IND, application for human clinical testing, which must become effective before human clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before the clinical trial is commenced;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, GCP, requirements and other clinical-trial related regulations to establish the safety and efficacy of the proposed drug for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, after completion of all pivotal clinical trials, which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labeling;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of an NDA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed drug is produced to assess compliance with current GMP regulations and of selected clinical trial sites to assess compliance with GCPs; and
- FDA review and approval of the NDA to permit commercial marketing of the product for particular indications for use in the United States.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical and Clinical Development

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs. The results of preclinical testing are submitted to the FDA as part of an IND application along with other information, including information about the product candidate, chemistry, manufacturing and controls, any available human data or literature to support the use of the product candidate and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day period, raises safety concerns or questions relating to one or more proposed clinical trials and places the clinical trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns, non-compliance or other issues affecting the integrity of the trial. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence and, once begun, issues may arise that could cause the trial to be suspended or terminated.

Clinical trials involve the administration of the investigational drug product to human subjects under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCP, an international standard meant to protect the rights and health of clinical research participants and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on United States patients and subsequent protocol amendments must be submitted to the FDA as part of the IND. Furthermore, an

independent IRB or ethics committee for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits.

Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objects. The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements. Further, an IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions. Some trials also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may recommend a clinical trial to be halted if it determines that there is an unacceptable safety risk for subjects or other grounds, such as futility.

Clinical trials to support an NDA for marketing approval are typically conducted in three sequential phases, but the phases may overlap or be combined. In Phase 1 clinical trials, the investigational product is typically introduced into a limited population of healthy human subjects or patients with the target disease or condition. These trials are designed to test the safety, dosage tolerance, pharmacokinetics and pharmacological actions of the investigational product, to identify side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. Phase 2 clinical trials usually involve administering the investigational product to a limited patient population with the specified disease or condition to evaluate the preliminarily efficacy, dosage tolerance, and optimum dosage, and to identify possible adverse effects and safety risks. Phase 3 clinical trials are typically undertaken in a larger number of patients, typically at geographically dispersed clinical trial sites, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse patient population. These clinical trials are intended to permit the FDA to evaluate the overall benefit-risk relationship of the investigational product and to provide adequate information for the labeling of the product candidate.

In reviewing an NDA, the FDA will consider all information submitted in the NDA, including the results of all clinical trials conducted. In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the NDA. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication and further document clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in the withdrawal of approval for products.

Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with current GMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the product candidate, findings from animal or in vitro testing that suggest a significant risk for human subjects, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure.

NDA submission and review

Assuming successful completion of the required clinical testing in accordance with all applicable regulatory requirements, an NDA application which includes, among other information, the results of product development, preclinical studies and clinical trials are submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include, among other things, the results of all trials and preclinical testing, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, controls and proposed labeling. The cost of preparing and submitting an NDA is substantial. The submission of most NDAs is additionally subject to a substantial application user fee, unless a waiver or exemption applies, currently $2,875,842, as well as an annual program fee, currently $336,432. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA to either issue a Refuse to File Letter or accept the NDA for filing, indicating that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing, but this timeframe can be extended such as by the submission of major amendments by applicants during the review period. The FDA reviews an NDA to determine, among other things, whether the product is safe and effective and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency.

The FDA may refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCPs. Additionally, the FDA will inspect the facility or the facilities at which the proposed product is manufactured. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates the NDA and conducts inspections of the manufacturing facilities where the investigational product and/or its drug substance will be produced, it issues either an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the drug with approved prescribing information for specific indications. A Complete Response letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response letter generally outlines the deficiencies in the submission, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may require substantial additional clinical data and/or other significant, expensive, and time-consuming requirements related to clinical trials, preclinical studies and/or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, withdraw the application or request a hearing. The FDA has committed to reviewing resubmissions of the NDA addressing such deficiencies in two or six months depending on the type of information included. Even if such data are submitted, however, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If regulatory approval of a product is granted, such approval will be granted for a particular indication(s) and may include limitations on the indicated use(s) for which such product may be marketed. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to

assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for REMS can materially affect the potential market and profitability of the product. Moreover, product approval may also be conditioned on substantial post-approval testing, such as Phase 4 post-market studies, and surveillance to monitor the product's safety or efficacy, and FDA may limit further marketing of the product based on the results of these post-approval studies. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

505(b)(2) NDA Approval Process

Section 505(b)(2) of the FDCA provides an alternate regulatory pathway for the FDA to approve a new product and permits reliance for such approval on published literature or an FDA finding of safety and effectiveness for a previously approved drug product. Specifically, section 505(b)(2) permits the filing of an NDA where one or more of the investigations relied upon by the applicant for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference. Typically, 505(b)(2) applicants must perform additional trials to support the change from the previously approved drug and to further demonstrate the new product's safety and effectiveness. The FDA may then approve the new product candidate for all or some of the labeled indications for which the referenced product has been approved, as well as for any new indication sought by the section 505(b)(2) applicant.

Regulation of Combination Products in the United States

Certain products may be comprised of components, such as drug components and device components, that would normally be regulated under different types of regulatory authorities, and frequently by different centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- a product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- two or more separate products packaged together in a single package or as a unit and comprised of drug and device products, device and biological products, or biological and drug products;
- a drug, or device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, or device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
- any investigational drug, or device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Under the FDCA and its implementing regulations, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The designation of a lead center generally eliminates the need to receive approvals from more than one FDA component for combination products, although it does not preclude consultations by the lead center with other components of FDA. The determination of which center will be the lead center is based on the “primary mode of action” of the combination product. Thus, if the primary mode of action of a drug-device combination product is attributable to the drug product, the FDA center responsible for premarket review of the drug product would have primary jurisdiction for the combination product. The FDA has also established an Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible

for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute.

A combination product with a drug primary mode of action generally would be reviewed and approved pursuant to the drug approval processes under the FDCA. In reviewing the NDA application for such a product, however, FDA reviewers in the drug center could consult with their counterparts in the device center to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to current GMP requirements applicable to both drugs and devices, including the Quality System, or QS, regulations applicable to medical devices.

Post-approval requirements

Once an NDA is approved, a product will be subject to pervasive and continuing regulation by the FDA including, among other things, requirements relating to current GMPs, quality controls, record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the practice of medicine by physicians or their choice of treatments. The FDA does, however, regulate manufacturer's communications on the subject of off-label use of their products.

In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to current GMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA, and certain state agencies for compliance with current GMPs, which impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from current GMPs and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. NDA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to current GMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with current GMPs.

The FDA may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards or is not maintained, if problems occur following initial marketing, or if previously unrecognized problems are subsequently discovered. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a 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 applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

U.S. Patent Term Restoration

Depending upon the timing, duration and specifics of the potential FDA approval of AV-101 and any future product candidates, some of our U.S. patents may be eligible for limited patent term extension. The Hatch-Waxman Amendments permit a patent restoration term, often referred to as patent term extension, of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves or denies the application for any patent term extension or restoration. In the future, we intend to apply for extension of patent term for one of our patents covering AV-101 to add patent life beyond its current expected expiration date.

U.S. Marketing Exclusivity

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain marketing applications, including 505(b)(2) applications. The FDA provides three years of marketing exclusivity for an NDA (including a 505(b)(2) application), or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. Three-year exclusivity is typically awarded to innovative changes to a previously-approved drug product, such as new indications, dosage forms or strengths. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving applications for drugs that do not have the innovative change, such as generic copies of the original, unmodified drug product. Three-year exclusivity blocks approval of 505(b)(2) applications and abbreviated new drug applications, or ANDAs, but will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods, including exclusivity attaching to certain patent certifications. This six-month exclusivity, which runs from the end of other exclusivity protection and patent terms, may be granted based on the voluntary completion within certain timeframes of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

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—generally a disease or condition with either a patient population that affects fewer than 200,000 individuals in the United States or a patient population greater than 200,000 individuals in the United States and there is no reasonable expectation that the cost of developing and making available the drug will be recovered from sales of the drug in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the product and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same product for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of the patients with the disease or condition for which the product was designated. Orphan drug exclusivity does not prevent the FDA from approving a different product for the same disease or condition, or the same product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan drug designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Fast Track Designation, Breakthrough Therapy Designation and Accelerated Approval

The FDA is required to facilitate the development, and expedite the review, of drugs that are intended for the treatment of a serious or life-threatening disease or condition which demonstrate the potential to address unmet medical needs for the condition. These programs include fast track designation, priority review and accelerated approval.

A product candidate is eligible for fast track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. Under the fast track program, the sponsor of a drug candidate may request that the FDA designate the candidate for a specific indication as a fast track product concurrent with, or after, the filing of the IND for the candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. Fast track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review of sections of a the applicant's NDA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Under the FDA's breakthrough therapy program, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation comes with all of the benefits of fast track designation. The FDA may take other actions appropriate to expedite the development and review of the product candidate, including intensive guidance on an efficient product development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for marketing, including under the fast track or breakthrough designation program, may also be eligible for other types of FDA programs intended to expedite development and review, such as accelerated approval. Products are eligible for accelerated approval if they can be shown to have 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 an effect on 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.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4, or post-approval, clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies with diligence, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Priority Review

A product is eligible for priority review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. 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 Prescription Drug User Fee Act, or PDUFA, guidelines. Under the new 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.

Pediatric information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data 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 drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

Disclosure of clinical trial information

Sponsors of clinical trials of FDA-regulated products, including drugs and combination products, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

European Union—process

In the European Union, or EU, our product candidate(s) may also be subject to extensive regulatory requirements governing, among other things, clinical trials and any commercial sales and distribution of our product candidate(s).

Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities located in the EU member states prior to the commencement of clinical trials as well as EU or national regulatory approvals prior to marketing the product candidate(s).

Non-clinical studies and clinical trials

Similar to the United States, the various phases of non-clinical studies and clinical trials in the EU are subject to significant regulatory controls.

Non-clinical studies are performed to demonstrate the health or environmental safety of new chemical substances. Non-clinical studies must be conducted in compliance with the principles of good laboratory practice, or GLP, as set forth in EU Directive 2004/10/EC. In particular, non-clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non-clinical studies. These GLP standards reflect the Organization for Economic Co-operation and Development requirements.

Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization, or ICH, guidelines on GCP, as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of

Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy, and in most EU member states, the sponsor is liable to provide 'no fault' compensation to any study subject injured in the clinical trial.

Although the EU Clinical Trials Directive 2001/20/EC has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the EU, the EU member states have transposed and applied the provisions of the Directive differently. This has led to significant variations in the member state regimes. Under the current regime, and similarly to the United States, before a clinical trial can be initiated in the EU a clinical trial application, or CTA, much like the IND must be submitted to each member state's national competent authority, or NCA, and independent ethics committee, or EC, where the trial is to be conducted. Once the CTA is approved by the NCA and the EC has granted a positive opinion in relation to the conduct of the trial in the relevant member state(s), in accordance with a country's requirements, clinical study development may proceed.

The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. Currently, CTAs must be submitted to the competent authority in each EU member state in which the trial will be conducted. The EU clinical trials legislation is currently undergoing a transition process mainly aimed at harmonizing and streamlining CTA, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. In April 2014, the EU adopted the EU Clinical Trials Regulation (EU) No 536/2014, or CTR, which is set to repeal the current EU Clinical Trials Directive 2001/20/EC. The CTR will be directly applicable in all member states. Under the CTR, which is currently expected to become applicable by early 2022, there will be a centralized application procedure where one national authority takes the lead in reviewing the application and the other national authorities have only limited involvement. Any substantial changes to the trial protocol or other information submitted with the CTA must be notified to or approved by the NCAs and ECs. Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU-wide regulatory requirements may also apply. All suspected unexpected serious adverse reactions to the investigational drug that occur during the clinical trial have to be reported to the NCA of the member state where they occurred.

Disclosure of clinical trial information

In the EU, under the EU Clinical Trials Directive, sponsors of clinical trials must specifically disclose (i) the summary results of adult clinical trials conducted (wholly or partially) in the EU within 12 months of completion of the trial; and (ii) the summary results of pediatric clinical trials, even when conducted outside the EU but included in a pediatric investigation plan, or PIP, within 6 months of completion of the trial.

The CTR will significantly enlarge the publication and transparency obligations for clinical trial sponsors. Additionally, the CTR requires that EU member states adopt specific measures, including penalties, to adequately sanction infringements of the relevant transparency obligations.

Marketing Authorizations

In the EU, medicinal products can only be placed on the market after obtaining a marketing authorization, or MA. To obtain regulatory approval of an investigational medicinal product under EU regulatory systems, we must submit a marketing authorization application, or MAA. The process for doing this depends, among other things, on the nature of the medicinal product.

Centralized procedure

Under the centralized procedure, the European Commission issues a single MA, based on the opinion of the European Medicines Agency's, or EMA, Committee for Human Medicinal Products, or CHMP, which is valid across the entire territory of the EU, as well as Iceland, Liechtenstein and Norway (i.e. the European Economic Area, or EEA). The centralized procedure is compulsory for human medicines that are: (i) derived from biotechnology processes; (ii) advanced-therapy medicinal products (i.e. gene therapy, somatic cell-therapy or tissue-engineered medicines); (iii) contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative diseases, viral diseases or autoimmune diseases and other immune dysfunctions; and (iv) officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized MA to the EMA, if the product contains a new active substance not yet authorized in the EU, or

the medicine concerned is a significant therapeutic, scientific or technical innovation, or that the granting of authorization would be in the interest of public health at EU-level.

Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Clock stops may extend the timeframe of evaluation of a MAA considerably beyond 210 days. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a MA, which is issued within 67 days of receipt of the EMA's recommendations. In exceptional cases, accelerated assessment or a MAA might be performed by the CHMP in no more than 150 days (not including clock stops) but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that the application is no longer appropriate to conduct an accelerated assessment. Innovative products that target an unmet medical need and are expected to be of a major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the United States. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Product developers that benefit from PRIME designation can expect to be eligible for accelerated assessment but this is not guaranteed. The benefits of a PRIME designation include the appointment of a CHMP rapporteur before submission of a MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process.

National authorization procedures

There are also two other possible routes to authorize medicinal products in several member states. National MAs are issued by the NCAs of the EU member states and only cover their respective territory. They are available for products that fall outside the scope of the centralized procedure:

- *Decentralized procedure*. If the product has not received a national MA in any member state at the time of application, an applicant may apply for simultaneous MAA in more than one EU member states. EU member states. Under the decentralized procedure an identical dossier is submitted to the NCA of each of the member states in which the MA is sought, one of which is selected by the applicant as the Reference Member State.
- *Mutual recognition procedure*. Under the mutual recognition procedure, a medicine that has already been authorized in one EU member state, in accordance with the national procedures of that member state, can be recognized in another member state.

MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk-benefit balance.

Similar to the United States, there is a process for authorization of generic/biosimilar versions of innovator drug products authorized in the EU. Abridged applications for the authorization of generic/biosimilar versions of drugs authorized via the EU centralized procedure can be submitted to the EMA through the centralized procedure referencing the innovator's data.

Orphan Medicinal Products

The criteria for designating an "orphan medicinal product" in the EU are similar in principle to those in the United States. A medicinal product may be designated as orphan if (1) it is intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions; (2) either (a) such condition affects no more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU or, if such a method exists, the product in question would be of significant benefit to those affected by the condition.

In the EU, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers, and are, upon grant of a MA, orphan medicinal products are entitled to ten years of market exclusivity. During the ten-year market exclusivity period, the EMA cannot accept a MAA, or grant a MA, or accept an application to extend a MA, for the same indication, in respect of a similar medicinal product. The applicant

will receive a fee reduction for the MAA if the orphan drug designation has been granted, but not if the designation is still pending at the time the MAA is submitted. An orphan product can also obtain an additional two years of market exclusivity in the EU for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The 10 year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. At any time, MA may be granted to a “similar medicinal product” for the same therapeutic indication if: (i) a second applicant can establish that its product, although similar to the authorized product, is safer, more effective or otherwise clinically superior; (ii) the MA holder for the authorized product consents to a second orphan medicinal product application; or (iii) the MA holder for the authorized product cannot supply enough orphan medicinal product. A “similar medicinal product” is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication.

Pediatric Development

In the EU, MAAs for new medicinal products have to include the results of trials conducted in the pediatric population, in compliance with a PIP agreed with the EMA's Pediatric Committee, or PDCO. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states and study results are included in the product information, even when negative, the product is eligible for a six-months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted.

The aforementioned EU rules are generally applicable in the EEA.

Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti-corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

Regulation of Combination Products

The EU regulates medical devices and medicinal products separately, through different legislative instruments, and the applicable requirements will vary depending on the type of drug-device combination product. EU guidance has been published to help manufacturers select the right regulatory framework. In the case of drug-delivery products intended to administer a medicinal product (and in which case the device and the medicinal product do not form a single integral product), the medicinal product is regulated in accordance with the aforementioned rules while the device part is regulated as a medical device and will have to comply with all the requirements set by the EU Council Directive 93/42/EEC, or the Medical Devices Directive.

The characteristics of non-integral devices used for the administration of medicinal products may impact the quality, safety and efficacy profile of the medicinal products. To the extent that administration devices are co-packaged with the medicinal product or, in exceptional cases, where the use of a specific type of administration device is specifically provided for in the product information of the medicinal product, additional information may need to be provided in the MAA for the medicinal product on the characteristics of the medical device(s) that may impact on the quality, safety and/or efficacy of the medicinal product. The

requirements regarding quality aspects for non-integral drug-device combination products, including devices that are co-packaged with medicinal products, are outlined in an EMA guideline of May 29, 2019, which currently remains in draft form.

The EU requires that all medical devices placed on the market in the EU must meet the relevant essential requirements laid down in Annex I of the Medical Devices Directive. The most fundamental essential requirement is that a medical device must be designed and manufactured in such a way that it will not compromise the clinical condition or safety of patients, or the safety and health of users and others. In addition, the device must achieve the performances intended by the manufacturer and be designed, manufactured, and packaged in a suitable manner. To demonstrate compliance with the essential requirements laid down in Annex I to the Medical Devices Directive, medical device manufacturers must undergo a conformity assessment procedure, which varies according to the type of medical device and its (risk) classification. Conformity assessment procedures require an assessment of available clinical evidence, literature data for the product, and post-market experience in respect of similar products already marketed. Except for low-risk medical devices (Class I non-sterile, non-measuring devices), where the manufacturer can self-declare the conformity of its products with the essential requirements (except for any parts which relate to sterility or metrology), a conformity assessment procedure requires the intervention of a Notified Body. Notified Bodies are independent organizations designated by EU countries to assess the conformity of devices before being placed on the market. If satisfied that the relevant product conforms to the relevant essential requirements, the Notified Body issues a certificate of conformity, which the manufacturer uses as a basis for its own declaration of conformity. The manufacturer may then apply the CE Mark to the device, which allows the device to be placed on the market throughout the EU.

As a general rule, demonstration of conformity of medical devices and their manufacturers with the essential requirements must be based, among other things, on the evaluation of clinical data supporting the safety and performance of the products during normal conditions of use. Specifically, a manufacturer must demonstrate that the device achieves its intended performance during normal conditions of use, that the known and foreseeable risks, and any adverse events, are minimized and acceptable when weighed against the benefits of its intended performance, and that any claims made about the performance and safety of the device are supported by suitable evidence.

On May 25, 2017, Regulation 2017/745, or the EU Medical Devices Regulation, entered into force, which repeals and replaces the Medical Devices Directive. The Medical Devices Regulation, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for medical devices and ensure a high level of safety and health while supporting innovation. Unlike the Medical Devices Directive, the Medical Devices Regulation includes some requirements for drug-device combination products but only for those designed and sold with a medicinal product as an integral part.

The Medical Devices Regulation was originally intended to become applicable three years after publication, but in April 2020 the transition period was extended by the European Parliament and the Council of the EU by an additional year—until May 26, 2021. Devices lawfully placed on the market pursuant to the Medical Devices Directive prior to May 26, 2021 may generally continue to be made available on the market or put into service until May 26, 2025. Once applicable, the new regulations will among other things:

- strengthen the rules on placing devices on the market and reinforce surveillance once they are available;
- establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number;
- set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the European Union, or EU; and
- strengthen the rules for the assessment of certain high-risk devices, which may have to undergo an additional check by experts before they are placed on the market.

Brexit and the Regulatory Framework in the United Kingdom

In June 2016, the electorate in the United Kingdom, or UK, voted in favor of leaving the EU (commonly referred to as "Brexit"). Thereafter, in March 2017, the country formally notified the EU of its intention to

withdraw pursuant to Article 50 of the Lisbon Treaty and the UK formally left the EU on January 31, 2020. The transition period, during which EU pharmaceutical laws continued to apply to the UK, has expired on December 31, 2020. However, the EU and the UK have concluded a trade and cooperation agreement, or TCA, which is provisionally applicable since January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations.

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

Other international markets—drug approval process

In some international markets (*e.g.*, China or Japan), although data generated in United States or EU trials may be submitted in support of a MAA, additional clinical trials conducted in the host territory, or studying people of the ethnicity of the host territory, may be required prior to the filing or approval of MA within the country.

Pricing and reimbursement

In the United States and internationally, sales of products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability and level of reimbursement from third-party payors such as state and federal governments, managed care providers and private insurance plans. Substantial uncertainty exists as to the reimbursement status of newly approved healthcare products by third-party payors.

In the United States no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor by payor basis. Private third-party payors tend to follow Medicare coverage policies and payment limitations in setting their own reimbursement rate to a substantial degree, but also have their own methods and approval process apart from Medicare determinations. As a result, coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained. Factors payors consider in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Increasingly, third party payors are implementing cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and also the out-of-pocket obligations of member patients for such products. In addition, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is possible that future legislation in the United States and other jurisdictions could be enacted which could potentially impact the reimbursement rates for the products we are developing and may develop in the future and also could further impact the levels of discounts and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of products that, if successfully developed, we bring to market.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. In the EU, governments influence the price of medicinal products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Member states are free to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. Member states may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market, including volume-based arrangements, caps and reference pricing mechanisms. To obtain reimbursement or pricing approval, some of the member states may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies that are considered the local standard of care. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription medicines, has become very intense. It is increasingly common in many EU member states for MA holders to be required to demonstrate the pharmaco-economic superiority of their products as compared to products already subject to pricing and reimbursement in specific countries. In order for drugs to be evaluated positively under such criteria, pharmaceutical companies may need to re-examine, and consider altering, a number of traditional functions relating to the selection, study, and management of drugs, whether currently marketed, under development, or being evaluated as candidates for research and/or development.

Sales and marketing

Sales, promotion and other activities following product approval are subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the U.S. Department of Justice, and similar foreign, state, and local government authorities.

As described above, the FDA regulates all advertising and promotion activities for products under its jurisdiction both prior to and after approval. A company can make only those claims relating to safety and efficacy that are approved by the FDA in labeling. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patients. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

Healthcare Laws and Regulations

Pharmaceutical companies are also subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business that may constrain the financial arrangements and relationships through which we research, as well as sell, market and distribute any products for which we obtain marketing authorization. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, and transparency laws and regulations related to drug pricing and payments and other transfers of value made to physicians and other healthcare providers. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of operations, integrity oversight and reporting obligations, exclusion from participation in federal and state healthcare programs and responsible individuals may be subject to imprisonment.

Similar rigid restrictions are imposed on the promotion and marketing of medicinal products in the EU and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we are not directly responsible for the promotion and marketing of our products, inappropriate activity by our international distribution partners can have adverse implications for us.

Healthcare Reform and Legislation

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new technologies such as gene therapy and therapies addressing rare diseases such as those we are developing. In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell our products profitably. In particular, in 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, was enacted, which, among other things, subjected biologic products to potential competition by lower-cost biosimilars; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and will remain open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. We cannot predict what affect further changes to the ACA would have on our business, especially given the new administration.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers up to 2% per fiscal year, and, due to subsequent legislative amendments, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2021, unless additional Congressional action is taken. In addition, the American Taxpayer Relief Act of 2012 further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Moreover, the federal government and the individual states in the United States have become increasingly active in developing proposals, passing legislation and implementing regulations designed to control drug pricing, including price or patient reimbursement constraints, discounts, formulary flexibility, marketing cost disclosure and transparency measures. These new laws and the regulations and policies implementing them, as well as other healthcare-related measures that may be adopted in the future, could materially reduce our revenues and our ability to develop and commercialize our product candidates, if approved. Further, on May 30, 2018, 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.

Data Privacy and Security Laws

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality, and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including data

breach notification laws, health information privacy and security laws, including HIPAA and federal and state consumer protection laws and regulations (e.g., Section 5 of the Federal Trade Commission Act) that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. In addition, certain state and non-U.S. laws, such as the CCPA, CPRA and GDPR, govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to make compliance efforts more challenging, and can result in investigations, proceedings, or actions that lead to significant penalties and restrictions on data processing.

Other Laws and Regulatory Processes

We will become subject to a variety of financial disclosure and securities trading regulations as a public company in the United States, including laws relating to the oversight activities of the SEC and, following the listing of our capital stock on The Nasdaq Global Market, we will be subject to the regulations of The Nasdaq Global Market. In addition, the Financial Accounting Standards Board, or FASB, the SEC and other bodies that have jurisdiction over the form and content of our accounts, our financial statements and other public disclosure are constantly discussing and interpreting proposals and existing pronouncements designed to ensure that companies best display relevant and transparent information relating to their respective businesses.

Our international operations are subject to compliance with the Foreign Corrupt Practices Act, or the FCPA, which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We also may be implicated under the FCPA for activities by our partners, collaborators, CROs, vendors or other agents.

Our present and future business has been and will continue to be subject to various other laws and regulations. Various laws, regulations and recommendations relating to safe working conditions, laboratory practices, the experimental use of animals, and the purchase, storage, movement, import and export and use and disposal of hazardous or potentially hazardous substances used in connection with our research work are or may be applicable to our activities. Certain agreements entered into by us involving exclusive license rights or acquisitions may be subject to national or supranational antitrust regulatory control, the effect of which cannot be predicted. The extent of government regulation, which might result from future legislation or administrative action, cannot accurately be predicted.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Facilities

We currently do not lease any facilities as our entire organization works remotely. We plan to lease office space in the greater Boston, Massachusetts metropolitan area. We believe that suitable space will be available on commercially reasonable terms.

Employees

As of June 22, 2021, we had eight full-time employees, including three in research and development and five in general and administrative functions. We also contract with a number of consultants to supplement the efforts and responsibilities of our employees. None of our employees is subject to a collective bargaining agreement or represented by a labor or trade union. We believe that our relations with our employees are good.

MANAGEMENT

Executives and Directors

The following table sets forth the name, age and position of each of our executives and directors as of June 22, 2021.

NAME	AGE	POSITION
Executive Officers:		
Timothy P. Noyes	59	Chief Executive Officer and Director
Benjamin T. Dake, Ph.D.	45	President, Chief Operating Officer and Secretary
George A. Eldridge	58	Chief Financial Officer and Treasurer
Hunter Gillies, M.B.Ch.B.	55	Chief Medical Officer
Ralph Niven, Ph.D.	61	Chief Development Officer
Non-Employee Directors:		
Mark Iwicki[1][2]	54	Chairperson and Director
David Grayzel, M.D.[2][3]	53	Director
Maha Katabi, Ph.D.[1][2]	47	Director
Joshua Resnick, M.D.[1][3]	46	Director

(1) Member of our audit committee

(2) Member of our compensation committee

(3) Member of our nominating and corporate governance committee

The following is a biographical summary of the experience of our executive officers and directors. Each executive officer serves at the discretion of our board of directors and holds office until his or her successor is duly elected and qualified or until his or her earlier resignation or removal. There are no family relationships among any of our directors or executive officers.

Executive Officers

Timothy P. Noyes Mr. Noyes has served as our Chief Executive Officer since February 2021 and a member of our board of directors since April 2021. Prior to joining the Company, from October 2019 to February 2021, Mr. Noyes served as President and Chief Executive Officer and a member of the board of directors of Arcuate Therapeutics, Inc. From April 2006 to September 2019, Mr. Noyes served as a member of the board of directors of ArTara Therapeutics, Inc., publicly traded pharmaceutical company formerly known as Proteon Therapeutics, Inc., or Proteon. From April 2006 to January 2020, Mr. Noyes also served as President and Chief Executive Officer of Proteon, until Proteon completed its merger with ArTara Therapeutics Inc. From January 2002 to March 2006, Mr. Noyes served as Chief Operating Officer of Trine Pharmaceuticals, Inc., or Trine. Before joining Trine, Mr. Noyes held several management positions with GelTex Pharmaceuticals Inc. from 1996 to 2001, prior to its acquisition by Genzyme Corporation. After the acquisition, from 2001 to 2002, he held the positions of President, Renal Division and President, GelTex Pharmaceuticals. Prior to GelTex, he worked for several years at Merck & Co. across multiple roles in its hypertension and heart failure group and managed care division, and on its Vasotec and Prilosec products. Mr. Noyes received an A.B. from Harvard College and an M.B.A. from Harvard Business School. We believe Mr. Noyes is qualified to serve as a member of our board of directors because of his role with us and his extensive operational knowledge of, and executive level management experience in, the biopharmaceutical industry.

Benjamin T. Dake, Ph.D. Dr. Dake founded the Company and has served as our President since July 2018, our Chief Operating Officer since September 2020 and our Secretary since August 2020. He served as our Chief Executive Officer from July 2018 until February 2021, and served as a member of our board of directors from July 2018 to April 2021. Prior to joining our company, Dr. Dake served in a number of positions of ascending responsibility at the investment firm RA Capital Management, L.P. from September 2015 until December 2019, including as a Venture Associate and Venture Analyst. From 2007 to 2010, Dr. Dake conducted research holding the title of Technical Research Assistant II at Brigham and Women's Hospital at the Center

for Neurodegenerative Disease. Before working in science, Dr. Dake was employed by the Gallup Organization from 1992 to 2004 where he held various information technology related positions and was a founder of their internet data collection venture “g.” Dr. Dake received a B.S. and an M.S. from University of Nebraska-Lincoln and a Ph.D. in cell, molecular and development biology from Tufts University School of Medicine.

George A. Eldridge Mr. Eldridge has served as our Chief Financial Officer since March 2021. Prior to joining our company, from October 2020 to March 2021, Mr. Eldridge served as Senior Vice President and Chief Financial Officer of Lyndra Therapeutics, Inc., or Lyndra, after consulting with Lyndra since August 2020. Prior to joining Lyndra, from February 2020 to October 2020, Mr. Eldridge served as a consultant and acting Chief Financial Officer to Sollis Therapeutics Inc. From September 2013 to January 2020, Mr. Eldridge was Senior Vice President and Chief Financial Officer of Proteon. Prior to joining Proteon, from 2009 to 2013, Mr. Eldridge served as a consultant to various companies in the biotechnology industry, acting as a chief financial officer and providing advisory services. From September 2006 to March 2009, Mr. Eldridge was Chief Financial Officer of Targanta Therapeutics Corporation until its acquisition in 2009 by The Medicines Company. Before working at Targanta, Mr. Eldridge served as Chief Financial Officer of Therion Biologics Corporation, or Therion, from 2002 to 2006. Prior to Therion, Mr. Eldridge served as Chief Financial Officer of Curis, Inc. (previously Ontogeny, Inc.) and Boston Life Sciences, Inc. Prior to working in the biotechnology field, Mr. Eldridge was an investment banker at Kidder Peabody & Co, Inc. Mr. Eldridge holds a B.A. from Dartmouth College and an M.B.A. from the University of Chicago, Booth School of Business.

Hunter Gillies, M.B.Ch.B. Dr. Gillies has served as our Chief Medical Officer since May 2020 and was a consultant for the Company from June 2019 to April 2020. Dr. Gillies has more than 20 years’ experience in developing drugs to treat pulmonary vascular disease. Prior to joining the Company, Dr. Gillies consulted from 2015 to April 2020 with a number of biotechnology and biopharmaceutical companies working in the field of pulmonary arterial hypertension, or PAH, (Actelion Pharmaceuticals Ltd., PhaseBio Pharmaceuticals, Inc., and Altavant Sciences, Inc.), as well as with companies in the field of heart failure, including Cardurion Pharmaceuticals, Inc. From February 2010 to December 2015, Dr. Gillies was a Senior Director in clinical research at Gilead Sciences where he was responsible for leading the pulmonary vascular disease team and led the U.S. component of the AMBITION study, a clinical trial for patients suffering from PAH. Prior to Gilead, Dr. Gillies held a number of positions of increasing responsibility at Pfizer from 1998 until 2010 where he was responsible for clinical research trials in sexual health, cardiovascular disease, and pulmonary vascular disease, including overseeing the Revatio program, a drug approved for PAH. Dr. Gillies earned his M.B.Ch.B., M.Sc. and B.Sc. in Exercise Physiology from the University of Cape Town, South Africa, and his diploma in Sports Medicine from Queen Mary University in London.

Ralph Niven, Ph.D. Dr. Niven has served as our Chief Development Officer since July 2020, and was a consultant for the Company from May 2018 to April 2020. Since March 2017, Dr. Niven has also served as scientific and development advisor to the SPARK translational medicine program at Stanford University. From August 2012 to January 2017, Dr. Niven held the position of Principal Fellow at Novartis Pharmaceuticals Corporation, or Novartis, a biopharmaceutical company, and was responsible for the technical development of several early-stage inhalation programs. Prior to Novartis, Dr. Niven served as Chief Technology Officer from September 2007 to January 2012 for APT Pharmaceuticals, Inc., or APT, during which time APT completed a Phase III study of an inhaled formulation of cyclosporine for chronic rejection in lung transplantation. Prior to APT, Dr. Niven served as Senior Vice President of Preclinical Development for Windtree Therapeutics, Inc., formerly known as Discovery Laboratories, Inc. from 2001 to 2005 where he established and ran the company’s California R&D facility focusing on aerosol applications of a synthetic lung surfactant. Dr. Niven also held positions at Megabios Corp., a company focused on cell and gene therapy, Advanced Inhalation Research, Inc., a biopharmaceutical company subsequently acquired by Alkermes, Inc., where Dr. Niven facilitated the development of dry powder “porous” particles for inhalation, Amgen, Inc., a pharmaceutical company, as a research scientist developing biomolecules for delivery via the lungs. Dr. Niven holds a Ph.D. in Pharmaceutical Sciences from the University of Kentucky and has an undergraduate degree in Pharmacy from the University of Strathclyde and holds an M.B.A. in Healthcare from George Washington University.

Non-Employee Directors

Mark Iwicki Mr. Iwicki has served as Chairperson of our board of directors since February 2021. Mr. Iwicki has served as the Chief Executive Officer and Chairman of the board of directors of Kala Pharmaceuticals, Inc., or Kala, since March 2015 and as President since August 2017. Previously he served as Executive Chairman

of the board of directors of Kala from April 2015 to September 2015. Prior to joining Kala, Mr. Iwicki served as President and Chief Executive Officer of Civitas Therapeutics, Inc., or Civitas, a biopharmaceutical company, from January 2014 to October 2014. Prior to Civitas, Mr. Iwicki served as President and Chief Executive Officer at Blend Therapeutics, Inc., or Blend, a biopharmaceutical company, from December 2012 to January 2014. Prior to Blend, Mr. Iwicki was President and Chief Executive Officer of Sunovion Pharmaceuticals Inc. (formerly Sepracor Inc.), or Sunovion, a pharmaceutical company, from October 2007 to June 2012. Prior to joining Sunovion, Mr. Iwicki was Vice President and Business Unit Head at Novartis, a biopharmaceutical company, from March 1998 to October 2007. Prior to that, Mr. Iwicki held management positions at Astra Merck Inc. and Merck & Co., Inc. In addition to serving on our board of directors, Mr. Iwicki also currently serves on the board of directors of Akero Therapeutics, Inc., Merus N.V. and Pulmatrix Inc., and formerly served on the board of directors of Aimmune Therapeutics, Inc., all publicly-traded companies, and Nimbus Therapeutics, Inc, a privately-held biotech company. Mr. Iwicki holds a B.S. in Business Administration from Ball State University and an M.B.A. from Loyola University. We believe that Mr. Iwicki's extensive experience as a pharmaceutical industry leader managing all stages of drug development and commercialization in multiple therapeutic areas qualifies him to serve as a member of our board of directors.

David Grayzel, M.D. Dr. Grayzel has served as a member of our board of directors since August 2020. Dr. Grayzel joined Atlas Venture Inc. in June 2010 and has been a Partner since April 2014. Before that, Dr. Grayzel co-founded and served as Chief Executive Officer of Arteaus Therapeutics, LLC from June 2011 until it was acquired by Eli Lilly and Company in January 2014, served as co-founder and Chief Executive Officer of Annovation Biopharma, Inc. from May 2011 until it was acquired by The Medicines Company in February 2015, served as a founding board member of Delinia, Inc. from September 2015 until it was acquired by Celgene Corporation in January 2017, and served as a co-founder and a member of the board of directors of Cadent Therapeutics, Inc., until it was acquired by Novartis in December 2020. Dr. Grayzel is currently a co-founder and board member of Surface Oncology, a publicly traded biotechnology company, and served as its Chief Executive Officer from April 2014 to May 2015 and as Chairman of its board of directors from April 2014 to January 2017, and is a co-founder and board member of Q32 Bio. He also serves as a board member of Xilio Therapeutics and Affinia Therapeutics, and as a board observer at Day One Biopharmaceuticals. Dr. Grayzel serves on the board of directors of Acera School, Inc. (The Massachusetts School for Science, Creativity, and Leadership). He also serves as an advisor to several organizations including Memorial Sloan Kettering Cancer Center's (MSKCC) Technology Development Fund, the American Heart Association's One Brave Idea, and is on the Scientific Advisory Board of the Tri-TDI that includes Rockefeller University, MSKCC, and Cornell University. Dr. Grayzel received a B.A. in Psychology from Stanford University, an M.D. from Harvard Medical School, and completed his internship and residency training in Internal Medicine at Massachusetts General Hospital. We believe that Dr. Grayzel's experience working with and serving on the boards of directors of life sciences companies and his experience working in the venture capital industry qualify him to serve on our board of directors.

Maha Katabi, Ph.D. Dr. Katabi has served as a member of our board of directors since August 2020. Dr. Katabi has been a General Partner at Sofinnova Investments, a venture capital firm, since March 2020. She joined Sofinnova as a Partner in April 2019. Prior to joining Sofinnova, Dr. Katabi was a founding Managing Partner at Oxalis Capital, a venture capital firm, from August 2018 until April 2019. From September 2008 until January 2018, Dr. Katabi was an Investment Manager and later Partner, Private Equity at Sectoral Asset Management, an investment advisor exclusively focused on the global healthcare sector, where she was the portfolio manager of a family of funds investing in small cap and private biotech companies. Prior to joining Sectoral, Dr. Katabi was a Vice President at Ventures West from 2004 to 2008, where she focused on early-stage venture investments in the life sciences industry. She started her venture capital career in 1999 with T2C2 Capital Bio, a seed fund focused on university start-ups. Dr. Katabi has served as a member of the board of directors of several private companies, and currently serves as a director of Amplyx Pharmaceuticals, Inc., Gyroscope Therapeutics Limited, Northsea Therapeutics B.V., Quanta Therapeutics, Inc., and Vera Therapeutics, Inc. She received a Ph.D. in Pharmacology and a B.Sc. in Biology at McGill University and her CFA charter in 2011. We believe that Dr. Katabi is qualified to serve on our board of directors due to her experience as a biopharmaceutical and biotechnology public and private company investor.

Joshua Resnick, M.D. Dr. Resnick has served as a member of our board of directors since August 2020 and previously served as a member of our board of directors from October 2018 to February 2020. Dr. Resnick has served as a Managing Director at RA Capital Management, L.P., a life sciences investment advisor, since

October 2018. Dr. Resnick previously served as a Partner at SV Health Investors from January 2016 to September 2018 and as President and Managing Partner at MRL Ventures Fund, an early-stage therapeutics-focused corporate venture fund that he built and managed within Merck & Co., from 2014 to January 2016. Dr. Resnick is on staff in the Department of Emergency Medicine at Massachusetts General Hospital. Dr. Resnick has served on the board of directors of Vor Biopharma Inc. since February 2019 and previously served on the boards of directors of Kalvista Pharmaceuticals, Inc. and Avrobio, Inc. from November 2016 to September 2018 and July 2016 to September 2018, respectively. Dr. Resnick received a B.A. in chemistry from Williams College, an M.D. from the University of Pennsylvania School of Medicine and an M.B.A. from The Wharton School of Business. We believe that Dr. Resnick is qualified to serve on our board of directors due to his experience as a biopharmaceutical and biotechnology public and private company investor.

Composition of Our Board of Directors

Our board of directors consists of five members, each of whom are members pursuant to the board composition provisions of our amended and restated certificate of incorporation and agreements with our stockholders, and is chaired by Mark Iwicki. After the completion of this offering, the number of directors will be fixed by our board of directors, subject to the terms of our second amended and restated certificate of incorporation and amended and restated bylaws. Each of our current directors will continue to serve as a director until the election and qualification of his or her successor or until his or her earlier death, resignation or removal.

Our nominating and corporate governance committee and our board of directors may therefore consider a broad range of factors relating to the qualifications and background of nominees. Our nominating and corporate governance committee's and our board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through their established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape, professional and personal experiences and expertise relevant to our growth strategy. Our directors hold office until their successors have been elected and qualified or until their earlier resignation or removal. Our second amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in an annual election of directors and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Staggered Board

In accordance with the terms of our second amended and restated certificate of incorporation and our amended and restated bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three classes of directors and each director will be assigned to one of the three classes. At each annual meeting of the stockholders, one class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. The terms of the directors will expire upon the election and qualification of successor directors at the annual meeting of stockholders to be held during the years 2022 for Class I directors, 2023 for Class II directors and 2024 for Class III directors. Our current directors will be divided among the three classes as follows:

- the Class I directors will be Timothy Noyes and Mark Iwicki;
- the Class II director will be Joshua Resnick, M.D.; and
- the Class III directors will be Maha Katabi, Ph.D. and David Grayzel, M.D.

Our second amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering will provide that the number of our directors shall be fixed from time to time by a resolution of the majority of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Director Independence

Our common stock has been approved for listing on The Nasdaq Global Market, or Nasdaq. Under the Nasdaq listing rules, independent directors must comprise a majority of a listed company's board of directors within

twelve months from the date of listing. In addition, the Nasdaq listing rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and governance committees be independent within twelve months from the date of listing. Audit committee members must also satisfy additional independence criteria, including those set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Nasdaq listing rules, a director will only qualify as an "independent director" if, in the opinion of that company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.

In order to be independent for purposes of Rule 10A-3 under the Exchange Act and under the rule of Nasdaq, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board of directors committee: (1) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries, other than compensation for board of directors service; or (2) be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board of directors must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director, and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors undertook a review of the composition of our board of directors and 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 all members of our board of directors, except for Timothy P. Noyes, do not have a relationship 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 rules of Nasdaq. Mr. Noyes is not an independent director under these rules because he is our Chief Executive Officer. In making these determinations, our board of directors considered the relationships that each director has with us and all other facts and circumstances the board of directors deemed relevant in determining independence, including the potential deemed beneficial ownership of our capital stock by each director, including non-employee directors that are affiliated with certain of our major stockholders. Upon the completion of this offering and after the completion of the transition periods thereunder, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of Nasdaq and the rules and regulations of the SEC after the completion of the transition periods thereunder. There are no family relationships among any of our directors or executive officers.

Board of Directors Leadership Structure and Role in Risk Oversight

Currently, the role chairperson of our board of directors is separated from the role of Chief Executive Officer. Our Chief Executive Officer is responsible for recommending strategic decisions and capital allocation to the board of directors and to ensure the execution of the recommended plans. The chairperson of our board of directors is responsible for leading the board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort, and energy that the Chief Executive Officer is required to devote to his position in the current business environment, as well as the commitment required to serve as our chairperson, particularly as the board of directors' oversight responsibilities continue to grow. While our amended and restated bylaws and corporate governance guidelines will not require that our chairperson and Chief Executive Officer positions be separate, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time and demonstrates our commitment to good corporate governance.

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including those risks more fully discussed in the section titled "Risk Factors" appearing elsewhere in this prospectus. Management is responsible for the day-to-day management of risks we face, while our board of directors, as a whole and through its committees, has responsibility for the

oversight of risk management. In its risk oversight role, our board of directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

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

Committees of Our Board of Directors

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee, each of which has the composition and the responsibilities described below. Each committee will operate pursuant to a charter to be adopted by our board of directors and will be effective upon the effectiveness of the registration statement of which this prospectus forms a part. We believe that the composition and functioning of all of our committees will comply with the applicable requirements of Nasdaq, the Sarbanes-Oxley Act of 2002 and SEC rules and regulations that will be applicable to us. Our board of directors may from time to time establish other committees. We intend to comply with future requirements to the extent they become applicable to us.

Following the closing of this offering, the full text of our audit committee charter, compensation committee charter and nominating and corporate governance charter will be posted on the investor relations portion of our website at https://www.aerovatetx.com. We do not incorporate the information contained on or accessible through our corporate website into this prospectus, and you should not consider it a part of this prospectus.

Audit Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our audit committee will consist of Mark Iwicki, Maha Katabi, Ph.D. and Joshua Resnick, M.D., and will be chaired by Maha Katabi, Ph.D. The functions of the audit committee will include:

- appointing, approving the compensation of and assessing the independence of our independent registered public accounting firm;
- pre-approving auditing and permissible non-audit services and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the overall audit plan with our independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- coordinating the oversight and reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending based upon the audit committee's review and discussions with management and our independent registered public accounting firm whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- reviewing and discussing with management certain of our insurance programs;
- reviewing and discussing with management our information security and technology risks;

- preparing the audit committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related person transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

All members of our audit committee will meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the Nasdaq listing rules. Our board of directors has determined that Maha Katabi, Ph.D. qualifies as an "audit committee financial expert" within the meaning of applicable SEC regulations. In making this determination, our board of directors considered the nature and scope of experience that has previously had with public reporting companies, including Maha Katabi, Ph.D. Our board of directors has determined that Mark Iwicki and Maha Katabi, Ph.D. satisfy the relevant independence requirements for service on the audit committee set forth in the rules of the SEC and the Nasdaq listing rules. Due to his affiliation with RA Capital Management, Joshua Resnick, M.D. is not independent for purposes of audit committee membership under Rule 10-3A of the Exchange Act.

Under applicable Nasdaq rules, we are permitted to phase-in our compliance with the independence requirements for our audit committee. The phase-in periods with respect to director independence allow us to have only one independent member on our audit committee upon the listing date of our common stock, a majority of independent members on our audit committee within 90 days of the listing date and a fully independent audit committee within one year of the listing date. We are taking advantage of these phase-in rules with respect to Dr. Resnick's service on our audit committee, and we expect that by the first anniversary of our listing on Nasdaq, our audit committee will comply with the applicable independence requirements.

Both our independent registered public accounting firm and management will periodically meet privately with our audit committee.

Compensation Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our compensation committee will consist of David Grayzel, M.D., Maha Katabi, Ph.D. and Mark Iwicki, and will be chaired by Mark Iwicki. The functions of the compensation committee upon the completion of this offering, will include:

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

Each member of our compensation committee is a non-employee director, as defined in Rule 16b-3 promulgated under the Exchange act, and an outside director, as defined pursuant to Section 162(m) of the Internal Revenue Code of 1986, as amended, or the Code.

Nominating and Corporate Governance Committee

Upon the effectiveness of the registration statement of which this prospectus forms a part, our nominating and corporate governance committee will consist of David Grayzel, M.D. and Joshua Resnick, M.D. and will be chaired by David Grayzel, M.D. The functions of the nominating and corporate governance committee will include:

- developing and recommending to the board of directors criteria for board of directors and committee membership, including a priority in selecting board members who exhibit a record of professional accomplishment, an understanding of the competitive challenges facing our business and industry and experience that will foster growth into a clinical-stage pharmaceutical company;
- establishing procedures for identifying and evaluating board of director candidates, including nominees recommended by stockholders;
- reviewing the composition of the board of directors to ensure that it is composed of members containing the appropriate skills and expertise to advise us;
- identifying individuals qualified to become members of the board of directors;
- recommending to the board of directors the persons to be nominated for election as directors and to each of the board of directors' committees;
- developing and recommending to the board of directors a code of business conduct and ethics and a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may from time to time establish other committees.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee is, or has at any time during the prior three years been, one of our officers or employees. None of our executive officers currently serve, or have in the past fiscal year served, as a member of the board of directors or compensation committee of any entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee.

Code of Business Conduct and Ethics

Our board of directors intends to adopt, subject to and effective upon the effectiveness of the registration statement of which this prospectus forms a part, a Code of Business Conduct and Ethics in connection with this offering. The Code of Business Conduct and Ethics will apply to all of our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions.

We intend to disclose future amendments to certain provisions of our Code of Business Conduct and Ethics on our website identified below. Upon the completion of this offering, the full text of our Code of Business Conduct and Ethics will be posted on our website at https://www.aerovatetx.com. Information contained on our website is not incorporated by reference into this prospectus and should not be considered to be a part of this prospectus or the registration statement of which it forms a part.

Limitations on Liability and Indemnification Agreements

As permitted by Delaware law, provisions in our second amended and restated certificate of incorporation which will become effective immediately prior to the closing of this offering, and amended and restated bylaws which will become effective upon the effectiveness of this registration statement, limit or eliminate the personal liability of directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, a director exercise an informed business judgment based on all material information reasonably available to him or her. Consequently, a director will not be personally liable to us or our stockholders for monetary damages or breach of fiduciary duty as a director, except for liability for:

- any breach of the director’s duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;

- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not limit or eliminate our rights or any stockholder's rights to seek non-monetary relief, such as injunctive relief or rescission. These provisions will not alter a director's liability under other laws, such as the federal securities laws or other state or federal laws. Our second amended and restated certificate of incorporation that will become effective immediately prior to the closing of this offering also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Delaware law, our amended and restated bylaws to be effective upon the effectiveness of this registration statement will provide that:

- we will indemnify our directors, officers, employees and other agents to the fullest extent permitted by law;
- we must advance expenses to our directors and officers, and may advance expenses to our employees and other agents, in connection with a legal proceeding to the fullest extent permitted by law; and
- the rights provided in our amended and restated bylaws are not exclusive.

If Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director or officer, then the liability of our directors or officers will be so eliminated or limited to the fullest extent permitted by Delaware law, as so amended. Our amended and restated bylaws to be effective upon the effectiveness of this registration statement will also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in connection with their services to us, regardless of whether our amended and restated bylaws permit such indemnification. We have obtained such insurance.

In addition to the indemnification that will be provided for in our second amended and restated certificate of incorporation to be effective immediately prior to the closing of this offering and amended and restated bylaws to be effective upon the effectiveness of this registration statement, we plan to enter into separate indemnification agreements with each of our directors and executive officers, which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements may require us, among other things, to indemnify our directors and executive officers for some expenses, including attorneys' fees, expenses, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of his service as one of our directors or executive officers or any other company or enterprise to which the person provides services at our request. We believe that these provisions and agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

This description of the indemnification provisions of our second amended and restated certificate of incorporation to be effective immediately prior to the closing of this offering, our amended and restated bylaws to be effective upon the effectiveness of this registration statement and our indemnification agreements is qualified in its entirety by reference to these documents, each of which is attached as an exhibit to the registration statement of which this prospectus forms a part.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable.

There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

EXECUTIVE COMPENSATION

Executive Compensation Overview

The following discussion contains forward-looking statements that are based on our current plans, considerations, expectations and determinations regarding future compensation programs. The actual amount and form of compensation and the compensation policies and practices that we adopt in the future may differ materially from currently planned programs as summarized in this discussion.

The compensation provided to our named executive officers for the fiscal year ended December 31, 2020 is detailed in the Summary Compensation Table and accompanying footnotes and narrative that follow this section.

Our named executive officers for the fiscal year ended December 31, 2020 are:

- Benjamin T. Dake, Ph.D., our President, Chief Operating Officer and Secretary and former Chief Executive Officer*;
- Hunter Gillies, M.B.Ch.B., our Chief Medical Officer; and
- Ralph Niven, Ph.D., our Chief Development Officer.

*Dr. Dake served as our Chief Executive Officer until Mr. Noyes commenced employment with us in February 2021.

2020 Summary Compensation Table

The following table presents information regarding the total compensation awarded to, earned by, and paid to our named executive officers for services rendered to us in all capacities for the fiscal year ended December 31, 2020.

NAME AND PRINCIPAL POSITION	YEAR	SALARY ($)	BONUS ($)[1]	STOCK AWARDS ($)	OPTION AWARDS [2] ($)	NON-EQUITY INCENTIVE PLAN COMPENSATION ($)	ALL OTHER COMPENSATION ($)[6]	TOTAL ($)
Benjamin T. Dake, Ph.D.	2020	240,556	86,656	—	174,907	—	—	502,119
President, Chief Operating Officer and Secretary								
Hunter Gillies, M.B.Ch.B. [3]	2020	240,000	55,680	—	61,093	—	66,668	423,441
Chief Medical Officer								
Ralph Niven, Ph.D. [4]	2020	175,000	86,333[5]	—	60,863	—	111,000	433,196
Chief Development Officer								

(1) The amount reported represents discretionary bonuses approved by our Board in recognition of prior services.

(2) The amount reported represents the aggregate grant date fair value of the shares of stock option awarded to the named executive officers during the 2020 fiscal year, calculated in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718. In addition, the amount reported represents the incremental fair value as of the date of awards modified during 2020, which such incremental fair value is equal to $0.06 per share. Such grant date fair value does not take into account any estimated forfeitures. The assumptions used in calculating the grant date fair value and the incremental fair value of the stock option reported in this column are set forth in Note 7 to our financial statements included elsewhere in this prospectus. The amount reported in this column reflects the accounting cost for these stock option awards and does not correspond to the actual economic value that may be received by the named executive officers upon the vesting of the stock options or any sale of the shares.

(3) Dr. Gillies commenced employment with the Company in May 2020. The amount reported for his salary reflects the amount paid following his commencement of employment.

(4) Dr. Niven commenced employment with the Company in July 2020. The amount reported for his salary reflects the amount paid following his commencement of employment.

(5) The amount reported includes a signing bonus of $58,333.

(6) The amounts provided reflect amounts earned pursuant to the applicable named executive officer's consulting arrangements in effect during 2020 prior to commencing full-time employment with us.

Narrative to Summary Compensation Table

Base Salaries

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. 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. For 2020, the base salary for each of Dr. Dake, Dr. Gillies and Dr. Niven was $200,000 (increased to $300,000 effective August 2020), $360,000 and $350,000, respectively. In connection with this offering, we increased the base salaries for Dr. Dake, Dr. Gillies and Dr. Niven to $360,000, $419,000 and $368,000, respectively, effective upon the completion of this offering.

Bonuses

We pay discretionary cash bonuses to reward our executives for their performance over the fiscal year. In addition, our named executive officers are eligible to receive annual target performance bonuses based on the achievement of certain corporate performance goals, as further described below. We believe such bonuses properly incentivize our named executive officers and allow us to remain competitive within the marketplace. During 2020, each Dr. Dake, Dr. Gillies and Dr. Niven were entitled to receive a target bonus of up to 30%, 20% and 10% of his base salary, respectively. Based on our achievement of the applicable performance goals for 2020, each named executive officer earned the amounts set forth in the 2020 Summary Compensation Table above. In connection with this offering, we increased the target bonus percentages for each of our named executive officers to 40% of their base salaries, effective upon the completion of this offering.

Equity Compensation

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. During the year ended December 31, 2020, we granted awards of stock options pursuant to our 2018 Plan (described in further detail below) to each of the named executive officers, as described in more detail in the “Outstanding Equity Awards at 2020 Fiscal Year-End” table. In addition, in September 2020, we reduced the exercise price of outstanding, unexercised stock options to reflect the then-current fair market value and additionally extended the term of such options to ten years from the date of such reduction.

Employment Arrangements with Our Named Executive Officers

Employment Agreements Entered into in Connection with our IPO

In connection with this offering, we entered into new employment agreements with each of our named executive officers, which shall supersede any prior offer letters or consulting agreements previously entered into. The new employment agreements provide for standard terms of employment, including base salary, annual bonus potential and benefits eligibility. In addition, the new employment agreements provide for severance benefits for our named executive officers. In connection with a termination without Cause or resignation for Good Reason (each, as defined in such executive’s employment agreement) (a “Qualifying Termination”), our named executive officers shall be entitled to the following benefits, subject to the execution and nonrevocation of a release in favor of the Company: (i) nine months of base salary continuation and (ii) nine months of continued Company-paid COBRA continuation benefits. Upon a qualifying termination within 12 months following a change in control under the new employment agreements of the Company, our named executive officers shall be entitled to the following benefits, in lieu of the aforementioned entitlements: (i) 12 months of base salary and the target annual bonus for the year of termination, payable in lump sum, (ii) 12 months of continued Company-paid COBRA continuation benefits, and (iii) full accelerated vesting of all equity awards subject to time-based vesting conditions. If any payments would be subject to the excise tax imposed by Section 4999 of the Code, then such payments shall be reduced to avoid the imposition of such excise tax, provided, however, that such reduction shall only occur if the executive’s reduced payments, in the aggregate, are greater than the aggregate payments to be received by the executive absent such reduction but with the imposition of the excise tax.

Offer Letters in Effect Prior to the IPO

Benjamin T. Dake, Ph.D.

On November 4, 2019 the Company and Benjamin T. Dake, Ph.D. entered into an Offer Letter, or the Dake Offer Letter, which provides for an annual base salary, an annual bonus opportunity and eligibility to participate in our employee benefit plans. In addition, the Dake Offer Letter provided for an equity grant, representing 3% of our then fully-diluted capitalization, which such award would vest as follows: 10% would be vested as of the date of grant, with 25% of the remaining 90% vesting on the first anniversary of Dr. Dake's start date, followed by equal monthly vesting for three years thereafter, subject to acceleration in connection with a termination without "cause" within 12 months following a Change of Control (as defined in our 2018 Plan). In connection with the Dake Offer Letter, the Company and Dr. Dake also entered into an Employee Proprietary Information, Inventions Assignment, Non-Competition and Non-Solicitation Agreement.

Hunter Gillies, M.B.Ch.B.

On April 27, 2020 the Company and Hunter Gillies, M.B.Ch.B. entered into an Offer Letter, or the Gillies Offer Letter, which provides for an annual base salary, an annual bonus opportunity, and eligibility to participate in our employee benefit plans generally. In addition, the Gillies Offer Letter provided for an equity grant representing 1% of our then fully-diluted capitalization, which such award would vest as follows: 10% would be vested as of the date of grant, with 25% of the remaining 90% vesting on the first anniversary of Dr. Gillies' start date, followed by equal monthly vesting for three years thereafter, subject to acceleration in connection with a termination without "cause" within 12 months following a Change of Control (as defined in our 2018 Plan). In connection with the Gillies Offer Letter, the Company and Dr. Gillies also entered into an Employee Proprietary Information, Inventions Assignment, Non-Competition and Non-Solicitation Agreement.

Prior to the Gillies Offer Letter, the Company and Dr. Gillies maintained a Consulting Agreement, or the Gillies Consulting Agreement, pursuant to which Dr. Gillies provided the services as specified in Exhibit A to the Gillies Consulting Agreement and was compensated at a rate of $16,667 per month. In connection with the Gillies Consulting Agreement, Dr. Gillies also entered into a Confidential Disclosure Agreement.

Ralph Niven, Ph.D.

On April 26, 2020 the Company and Ralph Niven, Ph.D. entered into an Offer Letter, or the Niven Offer Letter, which provides for an annual base salary, an annual bonus opportunity, a $58,333.33 signing bonus and eligibility to participate in our employee benefit plans generally. In addition, the Niven Offer Letter provided for an equity grant representing 1% of our then fully-diluted capitalization, which such award would vest as follows: 10% would be vested as of the date of grant, with 25% of the remaining 90% vesting on the first anniversary of Dr. Niven's start date, followed by equal monthly vesting for three years thereafter, subject to acceleration in connection with a termination without "cause" within 12 months following a Change of Control (as defined in our 2018 Plan). In connection with the Niven Offer Letter, the Company and Dr. Niven also entered into an Employee Proprietary Information, Inventions Assignment, Non-Competition and Non-Solicitation Agreement.

Prior to commencing employment with us in May 2020, Dr. Niven provided consulting services under a Consulting Agreement, or the Niven Consulting Agreement, pursuant to which Dr. Niven was compensated at a rate of $23,750 per month.

Outstanding Equity Awards at 2020 Fiscal Year-End

The following table sets forth information concerning outstanding equity awards held by each of our named executive officers as of December 31, 2020. All equity awards set forth in the table below were granted under our 2018 Plan.

	OPTIONS AWARDS					
NAME	VESTING COMMENCEMENT DATE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) EXERCISABLE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) UNEXERCISABLE	EQUITY INCENTIVE PLAN AWARDS: NUMBER OF SECURITIES UNDERLYING UNEXERCISED UNEARNED OPTIONS (#)	OPTION EXERCISE PRICE ($)	OPTION EXPIRATION DATE
Benjamin T. Dake, Ph.D.	1/1/2020[1]	4,829	43,464		$ 1.74	9/3/2030
	8/1/2020[2]	—	72,325		$ 1.74	9/3/2030
Hunter Gillies, M.B.Ch.B.	5/1/2020[1]	1,609	14,488		$ 1.74	9/3/2030
	8/1/2020[2]	—	24,108		$ 1.74	9/3/2030
Ralph Niven, Ph.D.	6/1/2020[1]	—	14,488		$ 1.74	9/3/2030
	8/1/2020[2]	—	24,108		$ 1.74	9/3/2030

(1) 10% of the shares subject to the award were vested as of vesting commencement date, with 25% of the remaining 90% of the shares subject to the award vesting on the first anniversary of the vesting commencement date, followed by equal monthly installments for 36 months thereafter, subject to the named executive officer's continuous service relationship. This award shall immediately accelerate and vest in full upon termination of the named executive officer's service relationship (other than for cause) within 12 months following a change in control.

(2) 25% of the shares subject to the award shall vest on the first anniversary of the vesting commencement date, and the remaining shares subject to the option vest in equal monthly installments for 36 months thereafter, subject to continued service with us through the applicable vesting date.

IPO Grants

At the time of effectiveness of the registration statement of which this prospectus is a part, our board of directors will grant options to purchase shares of our common stock under the 2021 Plan (as defined below) to our named executive officers, with an exercise price equal to the initial public offering price per share. On such date, Dr. Dake, Dr. Gillies and Dr. Niven will be granted 180,800, 60,300 and 26,300 options to purchase shares of our common stock, respectively, which options will vest in 48 equal monthly installments over four years following the grant date, subject to each named executive officer's continued employment through each such vesting date.

Employee Benefit and Equity Compensation Plans

2021 Stock Option and Incentive Plan

Our 2021 Stock Option and Incentive Plan, or 2021 Plan, was adopted by our board of directors on June 17, 2021, and approved by our stockholders on June 17, 2021 and will become effective as of the date immediately prior to the date of the effectiveness of the registration statement of which this prospectus is a part. The 2021 Plan allows the board of directors' compensation committee to make equity-based incentive awards to our officers, employees, directors and other key persons (including consultants). The 2021 Plan will replace our 2018 Plan. Our 2021 Plan provides flexibility to our compensation committee to use various equity-based incentive awards as compensation tools to motivate our workforce.

We have initially reserved 2,600,000 shares of our common stock, or the Initial Limit, for the issuance of awards under the 2021 Plan. The 2021 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2022, by 4% of the outstanding number of shares of our common stock on the immediately preceding December 31 or such lesser number of shares as determined by our compensation committee, or the Annual Increase. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2021 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, reacquired by us prior to vesting, satisfied without any issuance of stock, expire or are otherwise terminated (other than by exercise) under each of the 2021 Plan and the 2018 Plan will be added back to the shares of common stock available for issuance under the 2021 Plan.

The maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the Initial Limit cumulatively increased on January 1, 2022 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 2,600,000 shares of common stock.

The 2021 Plan will be administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2021 Plan. Persons eligible to participate in the 2021 Plan will be those full or part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation committee in its discretion.

The 2021 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed 10 years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as it may determine. Stock appreciation rights entitle the recipient to shares of common stock, or cash, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of the common stock on the date of grant.

Our compensation committee may award shares of restricted common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2021 Plan. Unrestricted stock may be granted to participants in recognition of past services or other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant cash bonuses under the 2021 Plan to participants, subject to the achievement of certain performance goals.

The 2021 Plan provides that in the case of, and subject to, the consummation of a “sale event” as defined in the 2021 Plan, all outstanding awards may be assumed, substituted or otherwise continued by the successor entity. To the extent that the successor entity does not assume, substitute or otherwise continue such awards, then (i) all stock options and stock appreciation rights will automatically become fully exercisable and the restrictions and conditions on all other awards with time-based conditions will automatically be deemed waived, and awards with conditions and restrictions relating to the attainment of performance goals may become vested and non-forfeitable in connection with a sale event in the compensation committee’s discretion and (ii) upon the effectiveness of the sale event, the 2021 Plan and all awards will automatically terminate. In the event of such termination, (a) individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights (to the extent exercisable) prior to the sale event; or (b) we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights (to the extent exercisable).

Our board of directors may amend or discontinue the 2021 Plan and our compensation committee may amend the exercise price of options and amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such action may adversely affect rights under an award without the holder’s consent. Certain amendments to the 2021 Plan require the approval of our stockholders.

No awards may be granted under the 2021 Plan after the date that is ten years from the date of stockholder approval. No awards under the 2021 Plan have been made prior to the date of this prospectus.

2018 Equity Incentive Plan

Our 2018 Equity Incentive Plan, or 2018 Plan, was approved and adopted by our board of directors and stockholders on August 3, 2018. As of June 22, 2021, we have reserved for issuance an aggregate of

2,189,774 shares of our common stock for the issuance of stock options and other equity awards under the 2018 Plan. This number of shares of common stock reserved for issuance is subject to adjustment in the event of a reverse stock split, stock dividend, extraordinary cash dividend, recapitalization, reorganization, merger, consolidation, combination, exchange of shares, liquidation, spin-off, split-up, or other similar change in capitalization or similar event. As of June 22, 2021, options to purchase 1,938,954 shares of common stock were outstanding under the 2018 Plan. Our board of directors has determined not to make any further awards under the 2018 Plan following the closing of this offering, but all outstanding awards under the 2018 Plan will continue to be governed by their existing terms. As of June 22, 2021, the maximum number of shares that may be issued as incentive stock options may not exceed 2,189,774 from the 2018 Plan.

The shares of common stock underlying any awards that are forfeited, surrendered, reacquired by us, expire, or are otherwise terminated (other than by exercise) under the 2018 Plan will be added back to the shares of common stock available for issuance under the 2021 Plan.

Our board of directors has acted as administrator of the 2018 Plan. The administrator has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of our 2018 Plan. Persons eligible to participate in our 2018 Plan will be those employees, officers, directors, consultants and advisors of the Company and our affiliates as selected from time to time by the administrator in its discretion.

Our 2018 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our board of directors (as defined in the 2018 Plan) but may not be less than 100% of the fair market value of our common stock on the date of grant, or in the case of an incentive stock option granted to a 10% owner, the exercise price shall not be less than 110% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our board of directors and may not exceed ten years from the date of grant. Our board of directors will determine at what time or times each option may be exercised.

Our board of directors may award restricted shares of common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and/or continued employment with us through a specified vesting period.

Our board of directors may also grant shares of common stock that are free from any restrictions under our 2018 Plan.

In the event of certain corporate transactions and events, including a stock split, reverse stock split, stock dividend, extraordinary cash dividend, recapitalization, reorganization, merger, consolidation, combination, exchange of shares, liquidation, spin-off, split-up, or other similar change in capitalization or similar event, the board of directors shall make appropriate adjustments to the maximum number of shares reserved for issuance under the 2018 Plan, the number and kind of securities subject to outstanding awards under the 2018 Plan and the repurchase or exercise price of any outstanding awards under the Plan.

Upon the effective time of a Change of Control (as defined in our 2018 Plan), our board of directors shall take any of the following actions or any combination thereof: (i) make appropriate provision for the continuation by the Company or the assumption and substitution of an award by the surviving or acquiring entity; (ii) accelerate the date of exercise or vesting of an award; (iii) permit the exchange of such award for the right to participate in any stock option or other employee benefit plan of any successor corporation; (iv) provide for the repurchase of an award for an amount equal to the difference of the per share transaction consideration minus any applicable per share exercise price of such award; or (v) provide for the termination of an award immediately prior to the consummation of the Change of Control, provided that no such termination will be effective if the Change of Control is not consummated.

No awards may be granted under our 2018 Plan after the date that is ten years from the effective date of our 2018 Plan.

Employee Stock Purchase Plan

On June 17, 2021, our board of directors adopted the Employee Stock Purchase Plan, or the ESPP, and on June 17, 2021, our stockholders approved the ESPP. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423(b) of the Code. The ESPP initially reserves and authorizes the issuance of up to a total of 230,000 shares of common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2022 and each January 1 thereafter through January 1, 2031, by the least of (i) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31, (ii) 460,000 shares or (iii) such number of shares as determined by the ESPP administrator. The number of shares reserved under the ESPP is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees whose customary employment is for more than 20 hours per week are eligible to participate in the ESPP. However, any participating employee who would own 5% or more of the total combined voting power or value of all classes of stock after an option were granted under the ESPP would not be eligible to purchase shares under the ESPP.

We will make one or more offerings each year to our employees to purchase shares under the ESPP. Offerings will usually begin on each January 1 and July 1 and will continue for six-month periods, referred to as offering periods. Each eligible employee may elect to participate in any offering by submitting an enrollment form at least 15 business days before the relevant offering date.

Each employee who is a participant in the ESPP may purchase shares by authorizing payroll deductions of up to 15% of his or her base compensation during an offering period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase shares on the last business day of the offering period at a price equal to 85% of the fair market value of the shares on the first business day or the last business day of the offering period, whichever is lower. Under applicable tax rules, an employee may purchase no more than $25,000 worth of shares of common stock, valued at the start of the purchase period, under the ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment with us for any reason.

Senior Executive Cash Incentive Bonus Plan

On June 17, 2021, our board of directors adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our board of directors or our compensation committee.

The payment targets will be related to financial and operational measures or objectives with respect to our company, or corporate performance goals, as well as individual performance objectives. Our board of directors or our compensation committee may select corporate performance goals from among the following: achievement of specified research and development, publication, clinical and/or regulatory milestones, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation and/or amortization), changes in the market price of our common stock, economic value-added, revenue, corporate revenue acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, stockholder returns, return on sales, gross or net profit levels, productivity, efficiency, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of stock, bookings, new bookings or renewals, sales or market shares; number of customers number of new customers or customer references; operating income and/or net annual recurring revenue, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, or as compared to results of a peer group, against the market as a whole, compared to applicable market indices and/or measured on a pre-tax or post-tax basis.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The corporate performance goals will be

measured at the end of each performance period after our financial reports have been published or such other appropriate time as the board of directors or the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. Subject to the rights contained in any agreement between the executive officer and us, an executive officer must be employed by us on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan also permits the board of directors or the compensation committee to adjust or approve additional bonuses to executive officers.

NON-EMPLOYEE DIRECTOR COMPENSATION

We did not pay any cash compensation, make any equity or non-equity awards to, or pay any other compensation to any of the non-employee members of our board of directors in 2020. During fiscal year 2020, Benjamin T. Dake, Ph.D., served as our President and Chief Executive Officer, as well as a member of our board of directors, and received no additional compensation for his services as a member of our board of directors. See the section titled "Executive Compensation" for more information about Dr. Dake's compensation for fiscal year 2020. We reimburse non-employee members of our board of directors for reasonable travel expenses incurred in attending meetings of our board of directors and committees of our board of directors.

Non-Employee Director Compensation Table—2020

	FEES EARNED OR PAID IN CASH ($)	OPTION AWARDS ($)[1]	ALL OTHER COMPENSATION ($)	TOTAL ($)
David Grayzel, M.D.	—	—	—	—
Mark Iwicki	—	—	—	—
Maha Katabi, Ph.D.	—	—	—	—
Jonathan Leff, M.D.[2]	—	—	—	—
Joshua Resnick, M.D.	—	—	—	—
Andrew Levin, M.D., Ph.D.[3]	—	—	—	—

(1) There were no options or other equity awards granted to directors in 2020. Except as noted below, none of our directors held options to purchase our common stock or any other stock awards as of December 31, 2020.

(2) Dr. Leff resigned from our board of directors, effective as of April 23, 2021.

(3) Dr. Levin resigned from our board of directors, effective as of August 5, 2020.

Non-Employee Director Compensation Policy

In connection with this offering, we intend to adopt a non-employee director compensation policy that will become effective upon the completion of this offering and will be designed to enable us to attract and retain, on a long-term basis, highly qualified non-employee directors. Under the policy, each director who is not an employee will be paid cash compensation from and after the completion of this offering, as set forth below:

	ANNUAL RETAINER
Board of Directors:	
Members	$ 35,000
Additional retainer for non-executive chair	$ 30,000
Audit Committee:	
Members (other than chair)	$ 7,500
Retainer for chair	$ 15,000
Compensation Committee:	
Members (other than chair)	$ 5,000
Retainer for chair	$ 10,000
Nominating and Corporate Governance Committee:	
Members (other than chair)	$ 4,000
Retainer for chair	$ 8,000

In addition, the non-employee director compensation policy will provide that, upon initial election to our board of directors, each non-employee director will be granted an option to purchase 25,000 shares of our common stock, or the Initial Grant. The Initial Grant will vest in equal monthly installments over three years from the date of grant, subject to continued service through the applicable vesting date. Furthermore, on the date of each annual meeting of stockholders following the completion of this offering, each non-employee

director who continues as a non-employee director following such meeting will be granted an annual option to purchase 12,500 shares of our common stock, or the Annual Grant. The Annual Grant will vest in full on the earlier of (i) the first anniversary of the grant date or (ii) our next annual meeting of stockholders, subject to continued service through the applicable vesting date. Such awards are subject to full accelerated vesting upon the sale of the company.

We will reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending meetings of the board of directors and committees thereof.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions or series of transactions since January 1, 2018, to which we were or will be a party, in which:

- the amount involved in the transaction exceeds, or will exceed, the lesser of $120,000 or one percent of the average of our total assets for the last two completed fiscal years; and
- in which any of our executive officers, directors or holders of five percent or more of any class of our capital stock, including their immediate family members or affiliated entities, had or will have a direct or indirect material interest.

Compensation arrangements for our named executive officers and our directors are described elsewhere in this prospectus under “Executive Compensation” and “Non-Employee Director Compensation.”

Private Placements of Securities

Common Stock

On July 27, 2018, we issued 241,467 shares of our common stock to RA Capital Healthcare Fund, L.P., or RA Healthcare, at a purchase price of $0.0012 per share. Joshua Resnick, M.D. serves on our board of directors and is an affiliate of RA Capital Management, L.P., or RA Capital, of which RA Healthcare is an affiliated fund. RA Healthcare and its affiliates collectively hold more than 5% of our voting securities.

Series Seed

On July 27, 2018, we issued 4,000,000 shares of our Series Seed convertible preferred stock at a purchase price of $1.00 per share to RA Healthcare. Joshua Resnick, M.D. serves on our board of directors and is an affiliate of RA Capital, of which RA Healthcare is an affiliated fund. RA Healthcare and its affiliates collectively hold more than 5% of our voting securities.

Convertible Note Financings

In December 2019, we issued convertible promissory notes, or the 2019 Notes, in an aggregate principal amount of $2.5 million. The 2019 Notes accrued interest at a rate of 6% per annum. The following table summarizes purchases of our 2019 Notes by related persons:

STOCKHOLDER	PRINCIPAL AMOUNT OF 2019 NOTES
Entities affiliated with RA Capital Management, L.P.[1]	$ 2,500,000

(1) Consists of (i) $1,604,577 in 2019 Notes issued to RA Healthcare, (ii) $270,423 in 2019 Notes issued to Blackwell Partners LLC—Series A, or Blackwell, and (iii) $625,000 in 2019 Notes issued to RA Capital Nexus Fund, L.P., or RA Nexus. Joshua Resnick, M.D. serves on our board of directors and is an affiliate of RA Capital, of which RA Healthcare, Blackwell and RA Nexus are affiliated funds. RA Healthcare, Blackwell and RA Nexus collectively hold more than 5% of our voting securities.

In July 2020, we issued convertible promissory notes, or the 2020 Notes, in the aggregate principal amount of $2.5 million. The 2020 Notes accrued interest at a rate of 3% per annum. The following table summarizes purchases of our 2020 Notes by related persons:

STOCKHOLDER	PRINCIPAL AMOUNT OF 2020 NOTES
Entities affiliated with RA Capital Management, L.P.[1]	$ 2,500,000

(1) Consists of (i) $1,689,822 in 2020 Notes issued to RA Healthcare, (ii) $185,178 in 2020 Notes issued to Blackwell and (iii) $625,000 in 2020 Notes issued to RA Nexus. Joshua Resnick, M.D. serves on our board of directors and is an affiliate of RA Capital, of which RA Healthcare, Blackwell and RA Nexus Fund are affiliated funds. RA Healthcare, Blackwell and RA Nexus collectively hold more than 5% of our voting securities.

In August 2020, in connection with our sale of Series A redeemable convertible preferred stock, the 2019 Notes and 2020 Notes converted into Series A redeemable convertible preferred stock. The 2019 Notes and

associated accrued interest converted into 1,700,343 shares of Series A redeemable convertible preferred stock at a conversion price of 80% of the Series A original issue price. The 2020 Notes converted into 1,320,655 shares of Series A redeemable convertible preferred stock at a conversion price of $1.893, the Series A original issue price.

Series A Redeemable Convertible Preferred Stock Financing

At closings on August 5, 2020, February 1, 2021 and June 4, 2021, we issued an aggregate of 37,031,156 shares of our Series A redeemable convertible preferred stock, at a purchase price of $1.893 per share pursuant to agreements entered into with investors, for an aggregate purchase price of approximately $70.1 million, excluding the issuance and subsequent conversion of the 2019 Notes and 2020 Notes. The following table summarizes purchases of our Series A redeemable convertible preferred stock by related persons as of June 22, 2021:

STOCKHOLDER	SHARES OF SERIES A PREFERRED STOCK	TOTAL PURCHASE PRICE
Entities affiliated with RA Capital Management, L.P.[1][2]	9,244,584	$ 17,499,997.55
Sofinnova Venture Partners X, L.P.[3]	10,565,238	$ 19,999,995.55
Atlas Venture Fund XII, L.P.[4]	7,976,754	$ 15,099,995.34
Entities affiliated with Cormorant Asset Management[5]	4,754,357	$ 8,999,997.83
Citadel Multi-Strategy Equities Master Fund Ltd.[6]	3,169,570	$ 5,999,996.02

(1) Consists of (i) 6,248,679 shares of Series A redeemable convertible preferred stock purchased by RA Healthcare, (ii) 684,758 shares of Series A redeemable convertible preferred stock purchased by Blackwell and (iii) 2,311,147 shares of Series A redeemable convertible preferred stock purchased by RA Nexus, and excludes the conversion of the 2019 Notes and 2020 Notes. Joshua Resnick, M.D. serves on our board of directors and is an affiliate of RA Capital Management, L.P., of which RA Healthcare, Blackwell and RA Nexus are affiliated funds. RA Healthcare, Blackwell and RA Nexus collectively hold more than 5% of our voting securities.

(2) Excludes approximately $5.7 million of aggregate principal amount, accrued interest and change in fair value of the 2019 and 2020 Notes, which was converted into an aggregate of 3,020,998 shares of our Series A redeemable convertible preferred stock.

(3) Sofinnova Venture Partners X, L.P., or Sofinnova, holds more than 5% of our voting securities, and Maha Katabi, Ph.D., an affiliate of Sofinnova, is a member of our board of directors.

(4) Atlas Venture Fund XII, L.P., or Atlas, holds more than 5% of our voting securities, and David Grayzel, M.D., an affiliate of Atlas, is a member of our board of directors.

(5) Consists of (i) 3,763,548 shares of Series A redeemable convertible preferred stock purchased by Cormorant Private Healthcare Fund II, LP, or Cormorant Private Healthcare and (ii) 990,809 shares of Series A redeemable convertible preferred stock purchased by Cormorant Global Healthcare Master Fund, LP, or Cormorant Global Healthcare. Cormorant Private Healthcare and Cormorant Global Healthcare collectively hold more than 5% of our voting securities.

(6) Citadel Multi-Strategy Equities Master Fund Ltd. holds more than 5% of our voting securities.

Agreements with Stockholders

In connection with our Series A redeemable convertible preferred stock financing, we entered into investors' rights agreement, voting agreement and right of first refusal and co-sale agreement containing registration rights, information rights, voting rights and rights of first refusal, among other things, with certain holders of our preferred stock and certain holders of our common stock. These stockholder agreements will terminate upon the closing of this offering, except for the registration rights granted under our investors' rights agreement, as more fully described in the section titled "Description of Capital Stock—Registration Rights."

Indemnification Agreements

In connection with this offering, we intend to enter into new agreements to indemnify our directors and executive officers. These agreements will, among other things, require us to indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person's status as a member of our board of directors to the maximum extent allowed under Delaware law.

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to this offering, the material

facts as to the related party's relationship or interest in the transaction were disclosed to our board of directors prior to their consideration of such transaction and the transaction was not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approved the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction are disclosed to the stockholders, who must approve the transaction in good faith.

In connection with this offering, we expect to adopt a written related party transactions policy that will provide that such transactions must be approved by our audit committee. This policy will become effective on the date on which the registration statement of which this prospectus forms a part is declared effective by the SEC. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving "related party transactions," which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director or greater than 5% beneficial owner of our common stock, in each case since the beginning of the most recently completed year and their immediate family members.

PRINCIPAL STOCKHOLDERS

The following table sets forth certain information known to us regarding beneficial ownership of our capital stock as of June 22, 2021, as adjusted to reflect the sale of common stock offered by us in this offering, for:

- each person or group of affiliated persons known by us to be the beneficial owner of more than five percent of our capital stock;
- each of our named executive officers;
- each of our directors; and
- all of our executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Under those rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power with respect to the securities as well as any shares of common stock that the individual or entity has the right to acquire within 60 days of June 22, 2021 through the exercise of stock options or other rights. These shares are deemed to be outstanding and beneficially owned by the person holding those options 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. Except as noted by footnote, and subject to community property laws where applicable, we believe, based on the information provided to us, that the persons and entities named in the table below have sole voting and investment power with respect to all common stock shown as beneficially owned by them.

Each individual or entity shown on the table has furnished information with respect to beneficial ownership. Unless otherwise indicated, the address for each beneficial owner is c/o Aerovate Therapeutics, Inc., 200 Berkeley Street, Floor 18, Boston, MA 02116.

The percentage of beneficial ownership prior to this offering in the table below is based on 14,425,930 shares of common stock deemed to be outstanding as of June 22, 2021, assuming the conversion of all outstanding shares of our preferred stock immediately prior to the completion of this offering, and the percentage of beneficial ownership after this offering in the table below is based on 23,108,072 shares of common stock outstanding after the closing of the offering. The information in the table below assumes no exercise of the underwriters' option to purchase additional shares.

NAME OF BENEFICIAL OWNER	NUMBER OF SHARES BENEFICIALLY OWNED	PERCENTAGE OF SHARES OUTSTANDING BENEFICIALLY OWNED	
		BEFORE OFFERING	AFTER OFFERING
Entities affiliated with RA Capital Management, L.P.[1]	5,478,268	38.0%	23.7%
Sofinnova Venture Partners X, L.P.[2]	3,401,544	23.6%	14.7%
Atlas Venture Fund XII, L.P.[3]	2,568,165	17.8%	11.1%
Entities affiliated with Cormorant Global[4]	1,530,691	10.6%	6.6%
Citadel Multi-Strategy Equities Master Fund Ltd.[5]	1,020,462	7.1%	4.4%
Named Executive Officers and Directors:			
Timothy P. Noyes[6]	—	—	—
Mark Iwicki[7]	8,140	*	*
David Grayzel, M.D.	—	—	—
Maha Katabi, Ph.D.	—	—	—
Joshua Resnick, M.D.	—	—	—
Benjamin T. Dake, Ph.D.[8]	57,892	*	*
George A. Eldridge[9]	—	—	—
Hunter Gillies, M.B.Ch.B.[10]	18,087	*	*
Ralph Niven, Ph.D.[11]	17,785	*	*
All executive officers and directors as a group (9 persons)[12]	101,904	*	*

* Less than one percent.

(1) Consists of (i) 241,467 shares of common stock, 1,287,825 shares issuable upon the conversion of the Series Seed convertible preferred stock and 2,650,562 shares issuable upon the conversion of the Series A redeemable convertible preferred stock held by RA Capital Healthcare Fund, L.P., or RA Healthcare, (ii) 987,244 shares issuable upon conversion of the Series A redeemable convertible preferred stock held by RA Capital Nexus Fund, L.P., or RA Nexus, and (iii) 311,170 shares issuable upon conversion of the Series A redeemable convertible preferred stock held by Blackwell Partners LLC—Series A, or Blackwell. RA Capital Management, L.P., or RA Capital is the investment manager for RA Healthcare, RA Nexus and Blackwell. The general partner of RA Capital is RA Capital Management GP, LLC, or RA Capital GP, of which Peter Kolchinsky and Rajeev Shah are the managing members. RA Capital, RA Capital GP, Peter Kolchinsky and Rajeev Shah may be deemed to have voting and investment power over the shares held of record by RA Healthcare, RA Nexus and Blackwell. RA Capital, RA Capital GP, Peter Kolchinsky, and Rajeev Shah disclaim beneficial ownership of such shares, except to the extent of any pecuniary interest therein. The address of RA Capital is 200 Berkeley Street, 18th Floor, Boston, Massachusetts 02116.

(2) Consists of 3,401,544 shares issuable upon the conversion of the Series A redeemable convertible preferred stock held by Sofinnova Venture Partners X, L.P., or Sofinnova X. Sofinnova Management X, L.L.C., or Sofinnova Management, is the general partner of Sofinnova X. Maha Katabi, Ph.D., together with James I. Healy and Michael F. Powell, are the managing members of Sofinnova Management. Such individuals and Sofinnova Management may be deemed to beneficially own the shares owned by Sofinnova X. Such individuals and Sofinnova Management expressly disclaim beneficial ownership over all shares except to the extent of any pecuniary interest therein. The address for Sofinnova X and Sofinnova Management is 3000 Sand Hill Road, Building 4, Suite 250, Menlo Park, California 94025.

(3) Consists of 2,568,165 shares issuable upon the conversion of the Series A redeemable convertible preferred stock held by Atlas Venture Fund XII, L.P., or Atlas Fund XII. The general partner of Atlas Fund XII is Atlas Venture Associates XII, L.P., or AVA XII LP. Atlas Venture Associates XII, LLC, or AVA XII LLC, is the general partner of AVA XII LP. David Grayzel, M.D. is a member of AVA XII LLC. Each of AVA XII LP, AVA XII LLC and Dr. Grayzel may be deemed to beneficially own the shares held by Atlas Fund XII. Each of AVA XII LP, AVA XII LLC and Dr. Grayzel expressly disclaim beneficial ownership of the securities owned by Atlas Fund XII, except to the extent of its pecuniary interest therein, if any. The address for AVA XII LP, AVA XII LLC and Atlas Fund XII is 300 Technology Sq., 8th Floor, Cambridge, MA 02139.

(4) Consists of (i) 1,211,696 shares of common stock issuable upon conversion of the Series A redeemable convertible preferred stock held by Cormorant Private Healthcare Fund II, LP, or Fund II, and (ii) 318,995 shares of common stock issuable upon conversion of the Series A redeemable convertible preferred stock held by Cormorant Global Healthcare Master Fund, LP, or Master Fund. Cormorant Global Healthcare GP, LLC and Cormorant Private Healthcare GP II, LLC serve as the general partners of the Master Fund and Fund II, respectively. Cormorant Asset Management, LP serves as the investment manager to the Master Fund and Fund II. Bihua Chen serves as the managing member of Cormorant Global Healthcare GP, LLC, Cormorant Private Healthcare GP II, LLC and the general partner of Cormorant Asset Management, LP. Each of the Reporting Persons disclaims beneficial ownership of the shares reported herein except to the extent of its or his pecuniary interest therein. The address for each of the entities is 200 Clarendon Street, 52nd Floor, Boston Massachusetts 02116.

(5) Consists of 1,020,462 shares issuable upon the conversion of the Series A redeemable convertible preferred stock held by Citadel Multi-Strategy Equities Master Fund Ltd., or Citadel. Citadel Advisors LLC, or Citadel Advisors, acts as the portfolio manager of Citadel. Citadel Advisors Holdings LP, or CAH, is the sole member of Citadel Advisors, and Citadel GP LLC, or CGP, is the general partner of CAH. Kenneth Griffin owns a controlling interest in CGP and may be deemed to share voting and dispositive power over shares held by Citadel. The address for this entity is c/o Citadel Advisors, 601 Lexington Avenue, New York, NY 10022.

(6) Consists of 747,634 shares subject to options held by Mr. Noyes, none of which are vested and exercisable within 60 days of June 22, 2021.

(7) Consists of 116,297 shares subject to options held by Mr. Iwicki, of which 8,140 shares are vested and exercisable within 60 days of June 22, 2021.

(8) Consists of 498,421 shares subject to options held by Dr. Dake, of which 57,892 shares are vested and exercisable within 60 days of June 22, 2021.

(9) Consists of 149,526 shares subject to options held by Mr. Eldridge, none of which are vested and exercisable within 60 days of June 22, 2021.

(10) Consists of 166,139 shares subject to options held by Dr. Gillies, of which 18,087 shares are vested and exercisable within 60 days of June 22, 2021.

(11) Consists of (i) 1,609 shares of common stock and (ii) 164,530 shares subject to options held by Dr. Niven, of which 16,176 are vested and exercisable within 60 days of June 22, 2021.

(12) Includes 1,609 shares of our common stock and options to purchase 100,295 shares of common stock exercisable within 60 days of June 22, 2021 held by our executive officers and directors, as described in notes six (6) through eleven (11) above.

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our second amended and restated certificate of incorporation, which will be effective upon the closing of this offering and amended and restated bylaws, which will be effective upon the effectiveness of the registration statement of which this prospectus is a part. The descriptions of the common stock and preferred stock give effect to changes to our capital structure that will occur immediately prior to the completion of this offering.

General

Upon completion of this offering, our authorized capital stock will consist of 150,000,000 shares of common stock, par value $0.0001 per share, and 10,000,000 shares of preferred stock, par value $0.0001 per share, all of which shares of preferred stock will be undesignated.

As of June 22, 2021, there were 14,425,930 shares of our common stock outstanding held of record by 10 stockholders, including the issuance of 29,338,346 shares of Series A redeemable convertible preferred stock at $1.893 per share since March 31, 2021, and assuming the automatic conversion of all outstanding shares of our convertible preferred stock into an aggregate of 14,182,854 shares of our common stock immediately prior to the closing of this offering, as if such conversion had occurred on June 22, 2021.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Upon the completion of this offering, all outstanding shares of our preferred stock will be converted into shares of our common stock. Upon the closing of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. Immediately after closing of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Registration Rights

Upon the completion of this offering, the holders of 14,182,854 shares of our common stock, including those issuable upon the conversion of preferred stock upon closing of this offering, will be entitled to rights with respect to the registration of these securities under the Securities Act (such shares are referred to herein as the “registrable securities”). These rights are provided under the terms of an investors’ rights agreement between us, certain holders of our common stock and holders of our preferred stock. The investors’ rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning 180 days after the effective date of this registration statement, the holders of 14,182,854 shares of our common stock, including those issuable upon the conversion of shares of our preferred stock upon closing of this offering are entitled to demand registration rights. Under the terms of the investors' rights agreement, we will be required, upon the written request of holders of at least 65% of the then outstanding shares of Series A redeemable convertible preferred stock (voting on an as converted into common stock basis) with respect to at least 35% of the registrable securities then outstanding (or a lesser percent if the anticipated aggregate offering price, net of related fees and expenses, would exceed $5 million), to file a registration statement covering such registrable securities. We are required to effect only two registrations pursuant to this provision of the investors' rights agreement.

Short-Form Registration Rights

Pursuant to the investors' rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of holders of at least 65% of the then outstanding shares of Series A redeemable convertible preferred stock (voting on an as converted into common stock basis) with respect to registrable securities having an anticipated aggregate offering price, net of related fees and expenses, of at least $1 million, we will be required to file a Form S-3 registration statement covering such registrable securities. We are required to effect only two registrations pursuant to this provision of the investors' rights agreement in any twelve-month period. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the investors' rights agreement, if we register any of our securities either for our own account or for the account of other security holders, the holders of our common stock, including those issuable upon the conversion of our preferred stock, are entitled to include their shares in the registration. Subject to certain exceptions contained in the investors' rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

Our investors' rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expenses of Registration

We will pay the registration expenses, subject to certain limited exceptions contained in the investors' rights agreement, of the holders of the shares registered pursuant to the demand, short-form and piggyback registration rights described above, including the expenses of one counsel for the selling holders.

Expiration of Registration Rights

The demand registration rights, short-form and piggyback registration rights granted under the investors' rights agreement will terminate upon the earliest to occur of: the closing of a deemed liquidation event (as defined in our existing amended and restated certificate of incorporation) or, as to any holder of registrable securities, at such time after this offering when all of such holder's shares may be sold without restriction pursuant to Rule 144 within a three month period.

Anti-Takeover Effects of Our Second Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws and Delaware Law

Certain provisions of the Delaware General Corporation Law and of our second amended and restated certificate of incorporation that will become effective upon the completion of this offering and amended and restated bylaws that will become effective upon the effectiveness of this registration statement could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our board of directors. These provisions might also have the effect of preventing changes in our management. It is possible

that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Board Composition and Filling Vacancies

Our second amended and restated certificate of incorporation will provide for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also will provide that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board of directors, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our second amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our amended and restated bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our second amended and restated certificate of incorporation and amended and restated bylaws will provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our amended and restated bylaws will establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our amended and restated bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our second amended and restated certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our second amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board of directors composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our second amended and restated certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our second amended and restated certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Choice of Forum

Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Chancery Court does not have jurisdiction, the federal district court for the District of Delaware or other state courts of the State of Delaware) will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our second amended and restated certificate of incorporation or amended and restated bylaws (including the interpretation, validity or enforceability thereof) or (4) any action asserting a claim governed by the internal affairs doctrine. Our amended and restated bylaws also provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our amended and restated bylaws is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

In addition, our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States will be the exclusive forum for any private action asserting violations by us or any of our directors or officers of the Securities Act or the Exchange Act, or the rules and regulations promulgated thereunder, and of all suits in equity and actions at law brought to enforce any liability or duty created by those statutes or the rules and regulations under such statutes. If any action the subject matter of which is within the scope of the preceding sentence is filed in a court other than the federal district courts of the United States, the plaintiff or plaintiffs shall be deemed by this provision of the amended and restated bylaws (i) to have consented to removal of the action by us to the federal district courts of the United States, in the case of an action filed in a state court, and (ii) to have consented to transfer of the action to the federal district courts of the United States.

We recognize that the Delaware Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims, particularly if the stockholders do not reside in or near the State of Delaware. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the United States may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

Delaware Anti-Takeover Statute

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which 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 commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of 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 provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Market Listing

Our common stock has been approved for listing on The Nasdaq Global Market under the trading symbol "AVTE."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 462 South 4th Street, Suite 1600, Louisville, KY 40202, and its telephone number is (877) 373-6374.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our shares, and although we expect that our common stock has been approved for listing on Nasdaq, we cannot assure investors that there will be an active public market for our common stock following this offering. Future sales of our common stock in the public market or the availability of such shares for sale in the public market could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of shares of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Upon completion of this offering, based on the number of shares outstanding as of June 22, 2021, 23,108,072 shares of our common stock will be outstanding, assuming the issuance of shares offered by us in this offering, no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options. Of the outstanding shares, all of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below, and restricted shares of common stock are subject to time-based vesting terms. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144 under the Securities Act. These restricted securities were issued and sold by us in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, summarized below.

As a result of the lock-up agreements and market stand-off provisions described below and the provisions of Rules 144 or 701 and no exercise of the underwriters' option to purchase additional shares, the shares of our common stock that will be deemed "restricted securities" will be available for sale in the public market following the completion of this offering as follows:

- 8,682,142 shares will be eligible for sale on the date of this prospectus; and
- 14,425,930 shares will be eligible for sale upon expiration of the lock-up agreements and market stand-off provisions described below, beginning more than 180 days after the date of this prospectus.

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately 231,080 shares immediately after this offering, assuming no exercise of the underwriters' option to purchase additional shares, based on the number of shares outstanding as of June 22, 2021; or
- the average weekly trading volume of our common stock on The Nasdaq Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the periodic reporting requirements of the Exchange Act for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written

compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares.

However, substantially all Rule 701 shares are subject to lock-up agreements as described below.

Lock-up Agreements

All of our directors and officers and the holders of substantially all of our capital stock and options have entered into lock-up agreements with us and have entered into or will enter into lock-up agreements with the underwriters and have agreed not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus continuing through the date 180 days thereafter, subject to certain exceptions. The representatives of the underwriters in this offering may, in their sole discretion, permit early release of shares subject to the lock-up agreements. See the section titled “Underwriting,” appearing elsewhere in this prospectus for more information.

Registration Rights

Upon completion of this offering, certain holders of our securities will be entitled to various rights with respect to registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section titled “Description of Capital Stock—Registration Rights” appearing elsewhere in this prospectus for more information.

Equity Incentive Plans

We intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our equity incentive plans. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the SEC. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of the date of this prospectus, we estimate that such registration statement on Form S-8 will cover approximately 4,768,954 shares. See the section titled “Executive Compensation—Employee Benefit Plans” appearing elsewhere in this prospectus for a description of our equity compensation plans.

MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following discussion is a summary of material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. For purposes of this discussion, a non-U.S. holder means a beneficial owner of our common stock that is, for U.S. federal income tax purposes:

- a non-resident alien individual;
- a corporation or any other organization taxable as a corporation for U.S. federal income tax purposes that is created or organized in or under laws other than the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is not subject to U.S. federal income tax on a net income basis; or
- a trust (1) that (a) has not made an election to be treated as a U.S. person under applicable U.S. Treasury regulations and (b) either (i) is not subject to the primary supervision of a court within the United States or (ii) is not subject to the substantial control of one or more U.S. persons or (2) the income of which is not subject to U.S. federal income tax on a net income basis.

This discussion does not address the tax treatment of partnerships or other entities or arrangements that are treated as pass-through entities for U.S. federal income tax purposes or persons that hold their shares of our common stock through partnerships or such other pass-through entities. The tax treatment of a partner in a partnership or other entity or arrangement that is treated as a pass-through entity for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partnership. A partner in a partnership or an investor in any other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of acquiring, holding and disposing of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the Code, existing and proposed U.S. Treasury regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and, all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any such change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance that the IRS will not challenge one or more of the tax consequences described herein. We assume in this discussion that a non-U.S. holder holds shares of our common stock as a “capital asset” within the meaning of Section 1221 of the Code, which is generally property held for investment.

This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder’s individual circumstances, including the alternative minimum tax, the Medicare tax on net investment income, the rules relating to “qualified small business stock,” any U.S. federal tax other than the income tax (including, for example, the estate or gift tax), or any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

1. insurance companies;
2. tax-exempt or governmental organizations;
3. financial institutions;
4. brokers or dealers in securities;
5. regulated investment companies;
6. pension plans;

7. “controlled foreign corporations,” “passive foreign investment companies,” and corporations that accumulate earnings to avoid U.S. federal income tax;
8. “qualified foreign pension funds,” or entities wholly owned by a “qualified foreign pension fund”;
9. persons deemed to sell our common stock under the constructive sale provisions of the Code;
10. persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment;
11. persons that hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
12. persons subject to special tax accounting rules as a result of any item of gross income with respect to the stock being taken into account in an applicable financial statement; and
13. U.S. expatriates.

This discussion is for general information only and is not tax advice. Accordingly, all prospective non-U.S. holders of our common stock should consult their tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

Distributions on Our Common Stock

As described in the “Dividend Policy” section above, we do not intend to pay any dividends in cash on our common stock to our stockholders in the foreseeable future. Distributions of cash, if any, on shares of our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a return of the non-U.S. holder’s investment, up to such holder’s adjusted tax basis in the shares of common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in “Gain on sale, exchange or other taxable disposition of shares of our common stock.” Any such distributions will also be subject to the discussion below under the section titled “Withholding and information reporting requirements—FATCA.”

Subject to the discussion in the following two paragraphs in this section, dividends paid to a non-U.S. holder generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends or such lower rate specified by an applicable income tax treaty between the United States and such holder’s country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same regular U.S. federal income tax rates applicable to United States persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional “branch profits tax” at a 30% rate or such lower rate as specified by an applicable income tax treaty between the United States and such holder’s country of residence.

A non-U.S. holder of shares of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder’s country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or a successor form) to the applicable withholding agent and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may generally obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Shares of Our Common Stock

Subject to the discussion below under “Withholding and information reporting requirements—FATCA,” a non-U.S. holder generally will not be subject to any U.S. federal income tax on any gain realized upon such holder’s sale, exchange or other taxable disposition of shares of our common stock unless:

1. the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed-base maintained by such non-U.S. holder in the United States, in which case the non-U.S. holder generally will be taxed on a net income basis at the regular U.S. federal income tax rates applicable to United States persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on our common stock" also may apply;

2. the non-U.S. holder is a nonresident alien individual who is present in the United States for a period or periods aggregating 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or

3. we are, or have been, at any time during the five-year period preceding such sale or other taxable disposition (or the non-U.S. holder's holding period, if shorter) a "United States real property holding corporation," unless our common stock is regularly traded on an established securities market, within the meaning of the relevant provisions of the Code, and the non-U.S. holder holds no more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "United States real property holding corporation" only if the fair market value of its "United States real property interests" (as defined in the Code and applicable U.S. Treasury regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a "United States real property holding corporation" for U.S. federal income tax purposes, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on shares of our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a United States person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on shares of our common stock. Generally, a non-U.S. holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable IRS Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above in "Distributions on our common stock," generally will be exempt from U.S. backup withholding.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of shares of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them. Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement. Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a

payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is filed with the IRS in a timely manner.

Withholding and Information Reporting Requirements—FATCA

The Foreign Account Tax Compliance Act, or FATCA, generally imposes a U.S. federal withholding tax at a rate of 30% on payments of dividends on our common stock paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," such foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," such foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA. Such withholding may also apply to payments of gross proceeds of sales or other dispositions of shares of our common stock, although under proposed U.S. Treasury regulations (the preamble to which specifies that taxpayers, including withholding agents, are generally permitted to rely on them pending finalization), no withholding will apply to payments of gross proceeds. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this paragraph. Non-U.S. holders should consult their tax advisors regarding the possible implications of this legislation on their investment in our common stock and the entities through which they hold our shares of common stock, including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated June 29, 2021, among us, and Jefferies LLC, Cowen and Company, LLC and Evercore Group L.L.C., as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

UNDERWRITER	NUMBER OF SHARES
Jefferies LLC	3,255,804
Cowen and Company, LLC	2,604,643
Evercore Group L.L.C.	2,170,535
Wedbush Securities Inc.	651,160
Total	8,682,142

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of $0.588 per share of common stock. After the offering, the initial public offering price and concession to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	PER SHARE		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES
Public offering price	$ 14.00	$ 14.00	$121,549,988	$139,782,482
Underwriting discounts and commissions paid by us	$ 0.98	$ 0.98	$ 8,508,499	$ 9,784,774
Proceeds to us, before expenses	$ 13.02	$ 13.02	$113,041,489	$129,997,708

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately $3.1 million. We have also agreed to reimburse the underwriters for certain of their expenses in an amount up to $50,000.

Determination of Offering Price

Prior to this offering, there has not been a public market for our common stock. Consequently, the initial public offering price for our common stock was determined by negotiations between us and the representatives. Among the factors considered in these negotiations were prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which the common stock will trade in the public market subsequent to the offering or that an active trading market for the common stock will develop and continue after the offering.

Listing

Our common stock has been approved for listing on Nasdaq under the trading symbol “AVTE”.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 1,302,321 shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter’s initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We, our officers, directors and holders of all or substantially all our outstanding capital stock have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer to sell, contract to sell or lend, effect any short sale or establish or increase a “put equivalent position” within the meaning of Rule 16a-l(h) under the Securities Exchange Act of 1934, as amended, or Exchange Act, liquidate or decrease a “call equivalent position” within the meaning of Rule 16a-l(h) under the Exchange Act, pledge, hypothecate or grant any security interest in, or otherwise dispose of, any shares of common stock, options or warrants or other rights to acquire shares of common stock or any securities exchangeable or exercisable for or convertible into shares of common stock, or to acquire other securities or rights ultimately exchangeable or exercisable for or convertible into shares of common stock, currently or hereafter owned either of record or beneficially (such shares and other securities referred to herein as “shares or related securities”), or
- enter into any swap, hedge or similar arrangement or agreement that transfers, in whole or in part, the economic risk of ownership of shares or related securities, regardless of whether any such transaction is to be settled in securities, in cash or otherwise, or

- make any demand for, or exercise any right with respect to, the registration under the Securities Act of the offer and sale of any shares or related securities, or cause to be filed a registration statement, prospectus or prospectus supplement (or an amendment or supplement thereto) with respect to any such registration, or
- publicly announce any intention to do any of the foregoing,

for a period of 180 days after the date of this prospectus without the prior written consent of Jefferies LLC and Cowen and Company, LLC. These restrictions terminate after the close of trading of the common stock on and including the 180th day after the date of this prospectus.

The restrictions in the immediately preceding paragraph do not apply to, subject to certain limitations:

- transactions relating to shares or related securities acquired in this offering or in open market transactions after the completion of this offering;
- transfers of shares or related securities by gift, including, without limitation, to a charitable organization, or by will or intestate succession to the legal representative, heir, beneficiary or any family member, or to a trust whose beneficiaries consist exclusively of one or more of such officer, director or holder and/or a family member thereof; provided however, that such transfer is not for consideration;
- transfers or dispositions of shares or related securities to a family member, a trust exclusively formed for the direct or indirect benefit of such officer, director or holder or a family member thereof or any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which, in each case, are held by such officer, director or holder or any family member; provided however, that such transfer is not for consideration;
- transfers of shares or related securities by operation of law pursuant to a qualified domestic order or other court order or in connection with a divorce settlement;
- distributions or transfers of shares or related securities to (x) another corporation, partnership, limited liability company, trust or other business entity that is a direct or indirect affiliate (as defined in Rule 405 promulgated under the Securities Act) of such officer, director or holder, (y) any investment fund or other entity controlling, controlled by, managing or managed by or under common control with the undersigned or affiliates of such officer, director or holder (including, for the avoidance of doubt, where the undersigned is a partnership, to its general partner or a successor partnership or fund, or any other funds managed by such partnership), or (z) limited partners, general partners, members, managers, managing members, stockholders or other equity holders of the undersigned or of the entities described in the preceding clauses (x) and (y);
- transfers or dispositions of shares of our common stock as forfeitures (x) to satisfy tax withholding and remittance obligations of the undersigned in connection with the vesting or exercise of equity awards granted pursuant to our equity incentive plans or (y) pursuant to a net exercise or cashless exercise by the stockholder of outstanding equity awards pursuant to our equity incentive plans;
- transfers of shares or related securities pursuant to a change of control (meaning the consummation of any bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of shares the result of which is that any “person” (as defined in Section 13(d)(3) of the Exchange Act), or group of persons, becomes the beneficial owner (as defined in Rules 13d-3 and 13d-5 of the Exchange Act) of more than 50% of our voting capital stock) after this offering that has been approved by the independent members of our board of directors, provided, that in the event that such change of control is not completed, the shares or related securities owned by such officer, director or holder shall remain subject to the restrictions herein;
- transfers or dispositions of shares or related securities pursuant to the exercise of an option to purchase shares granted under any of our equity incentive plans or stock purchase plans, in each case, that exist as of the date of this prospectus and are described in this prospectus relating to this offering, provided that the shares issued upon such exercise shall continue to be subject to the restrictions on transfer set forth in this letter agreement; or
- transfers of shares or related securities arising as a result of the termination of employment of such officer, director or holder to us pursuant to agreements that are in effect as of the date of this prospectus and disclosed in the prospectus, under which we have the option to repurchase such shares or related securities or a right of first refusal with respect to transfers of such shares or related securities.

Jefferies LLC and Cowen and Company, LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either “covered” short sales or “naked” short sales.

“Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

“Naked” short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The Nasdaq Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker’s bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters’ web sites and any

information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their respective affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses. We have entered into an agreement with Wedbush Securities Inc., an underwriter in this offering, for advisory services pursuant to which Wedbush Securities Inc. will receive an agreed-upon fee not to exceed 0.175% of the gross proceeds received by us from this offering.

In the ordinary course of their various business activities, the underwriters and certain of their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Disclaimers About Non-U.S. Jurisdictions

European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant State"), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which have been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that the shares may be offered to the public in that Relevant State at any time:

(a) to any legal entity which is a "qualified investor" as defined under Article 2 of the Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of representatives for any such offer; or

(c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of the shares shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation.

For the purposes of this provision, the expression "offer to the public" in relation to the shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

United Kingdom

No shares have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares which has been approved by the Financial Conduct Authority, except that the shares may be offered to the public in the United Kingdom at any time:

(a) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or

(c) in any other circumstances falling within Section 86 of the Financial Services and Markets Act of 2000, or FSMA,

provided that no such offer of the shares shall require the Issuer or any Manager to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any share and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Canada

(A) Resale Restrictions

The distribution of shares of common stock in Canada is being made only in the provinces of Ontario, Quebec, Alberta, British Columbia, Manitoba, New Brunswick and Nova Scotia on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of these securities are made. Any resale of the shares of our common stock in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the shares of common stock.

(B) Representations of Canadian Purchasers

By purchasing shares of our common stock in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase the shares of our common stock without the benefit of a prospectus qualified under those securities laws as it is an "accredited investor" as defined under National Instrument 45-106—*Prospectus Exemptions* or Section 73.3(1) of the *Securities Act* (Ontario), as applicable,
- the purchaser is a "permitted client" as defined in National Instrument 31-103—Registration Requirements, Exemptions and Ongoing Registrant Obligations,
- where required by law, the purchaser is purchasing as principal and not as agent, and
- the purchaser has reviewed the text above under Resale Restrictions.

(C) Conflicts of Interest

Canadian purchasers are hereby notified that certain of the underwriters are relying on the exemption set out in section 3A.3 or 3A.4, if applicable, of National Instrument 33-105—Underwriting Conflicts from having to provide certain conflict of interest disclosure in this document.

(D) Statutory Rights of Action

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if the prospectus (including any amendment thereto) such as this document contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser of these securities in Canada should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

(E) Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside

of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

(F) Taxation and Eligibility for Investment

Canadian purchasers of shares of common stock should consult their own legal and tax advisors with respect to the tax consequences of an investment in the shares of our common stock in their particular circumstances and about the eligibility of the shares of our common stock for investment by the purchaser under relevant Canadian legislation.

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;
- a person associated with the Company under Section 708(12) of the Corporations Act; and
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the securities issued to you pursuant to this prospectus for resale in Australia within 12 months of those securities being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

Hong Kong

No shares of our common stock have been offered or sold, and no shares of our common stock may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong, or the SFO, and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong, or the CO, or which do not constitute an offer or invitation to the public for the purpose of the CO or the SFO. No document, invitation or advertisement relating to the shares of our common stock has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the SFO and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the shares of our common stock may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the shares of our common stock will be required, and is deemed by the acquisition of the shares of our common stock, to confirm that he is aware of the restriction on offers of the shares of our common stock described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any shares of our common stock in circumstances that contravene any such restrictions.

Israel

This document does not constitute a prospectus under the Israeli Securities Law, 5728-1968, or the Securities Law, and has not been filed with or approved by the Israel Securities Authority. In Israel, this prospectus is being distributed only to, and is directed only at, and any offer of shares is directed only at, (i) a limited number of persons in accordance with the Israeli Securities Law and (ii) investors listed in the first addendum, or the

Addendum, to the Israeli Securities Law, consisting primarily of joint investment in trust funds, provident funds, insurance companies, banks, portfolio managers, investment advisors, members of the Tel Aviv Stock Exchange, underwriters, venture capital funds, entities with equity in excess of NIS 50 million and "qualified individuals," each as defined in the Addendum (as it may be amended from time to time), collectively referred to as qualified investors (in each case, purchasing for their own account or, where permitted under the Addendum, for the accounts of their clients who are investors listed in the Addendum). Qualified investors are required to submit written confirmation that they fall within the scope of the Addendum, are aware of the meaning of same and agree to it.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the common stock may not be circulated or distributed, nor may the common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares of our common stock are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; and
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor;

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares of our common stock pursuant to an offer made under Section 275 of the SFA except:

- to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- where no consideration is or will be given for the transfer;
- where the transfer is by operation of law;
- as specified in Section 276(7) of the SFA; or
- as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP. Certain legal matters related to this offering will be passed upon for the underwriters by Latham & Watkins LLP.

EXPERTS

The financial statements of Aerovate Therapeutics, Inc. as of December 31, 2019 and 2020, and for each of the years in the two-year period ended December 31, 2020, have been included herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the common stock we are offering by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the completion of this offering, we will be subject to the informational requirements of the Exchange Act and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, at the SEC's website at www.sec.gov. We also maintain a website at www.aerovatetx.com. Upon completion of this offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and any amendment to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

AEROVATE THERAPEUTICS, INC.
INDEX TO THE FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors
Aerovate Therapeutics, Inc.:

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Aerovate Therapeutics, Inc. (the Company) as of December 31, 2019 and 2020, the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows for each of the years in the two-year period ended December 31, 2020, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2020, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2020, in conformity with U.S. generally accepted accounting principles.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these 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. 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/ KPMG LLP

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

San Diego, California
May 6, 2021, except for the reverse stock split described in Note 1, which is as of June 22, 2021

AEROVATE THERAPEUTICS, INC.

BALANCE SHEETS
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	DECEMBER 31,	
	2019	2020
Assets		
Current assets:		
Cash	$ 3,514	$ 4,573
Prepaid expenses and other current assets	—	103
Total current assets	3,514	4,676
Property and equipment, net (Note 2)	—	39
Total assets	$ 3,514	$ 4,715
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable (including related party amounts of $3 and $6, respectively)	$ 542	$ 618
Accrued and other current liabilities (Note 3)	115	1,156
Total current liabilities	657	1,774
Convertible promissory notes to related party (Note 4)	2,500	—
Commitments and contingencies (Note 10)		
Series A redeemable convertible preferred stock, $0.0001 par value; 0 and 40,052,154 shares authorized at December 31, 2019 and 2020, respectively; 0 and 6,489,534 shares issued and outstanding at December 31, 2019 and 2020, respectively; aggregate liquidation preference of $12,285 at December 31, 2020	—	12,285
Series Seed redeemable convertible preferred stock, $0.0001 par value; 4,000,000 shares authorized, issued and outstanding at December 31, 2019 and 2020; aggregate liquidation preference of $4,000 at December 31, 2020	4,000	4,000
Stockholders' deficit:		
Common stock, $0.0001 par value; 5,000,000 and 50,000,000 shares authorized at December 31, 2019 and 2020, respectively; 241,467 and 243,076 shares issued and outstanding at December 31, 2019 and 2020, respectively	—	—
Additional paid-in capital	—	63
Accumulated deficit	(3,643)	(13,407)
Total stockholders' deficit	(3,643)	(13,344)
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	$ 3,514	$ 4,715

See accompanying notes to financial statements.

AEROVATE THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	YEARS ENDED DECEMBER 31,	
	2019	2020
Operating expenses:		
Research and development (includes related party amounts of $20 and $72, respectively)	$ 3,112	$ 7,940
General and administrative (includes related party amounts of $0 and $31, respectively)	218	949
Total operating expenses	3,330	8,889
Provision for income taxes	1	—
Loss from operations	(3,331)	(8,889)
Other income (expense):		
Interest expense	—	(75)
Change in fair value of convertible promissory notes	—	(644)
Other income (expense)	1	(3)
Total other income (expense)	1	(722)
Net loss and comprehensive loss	$ (3,330)	$ (9,611)
Net loss per share, basic and diluted	$ (13.79)	$ (40.31)
Weighted-average shares of common stock outstanding, basic and diluted	241,467	242,232

See accompanying notes to financial statements.

AEROVATE THERAPEUTICS, INC.

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
(IN THOUSANDS, EXCEPT SHARE AMOUNTS)

	SERIES A REDEEMABLE CONVERTIBLE PREFERRED STOCK		SERIES SEED REDEEMABLE CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' DEFICIT
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT			
Balance at December 31, 2018	—	$ —	4,000,000	$ 4,000	241,467	$ —	$ —	$ (313)	(313)
Net loss	—	—	—	—	—	—	—	(3,330)	(3,330)
Balance at December 31, 2019	—	—	4,000,000	4,000	241,467	—	—	(3,643)	(3,643)
Issuance of Series A redeemable convertible preferred stock upon conversion of December 2019 convertible promissory notes to related party	1,700,343	3,219	—	—	—	—	—	—	—
Issuance of Series A redeemable convertible preferred stock upon conversion of July 2020 convertible promissory notes to related party	1,320,655	2,500	—	—	—	—	—	—	—
Issuance of Series A redeemable convertible preferred stock at $1.893 per share, net of issuance costs of $153	3,468,536	6,413	—	—	—	—	—	—	—
Accretion of Series A redeemable convertible preferred stock to redemption value	—	153	—	—	—	—	—	(153)	(153)
Issuance of common stock upon exercise of stock options	—	—	—	—	1,609	—	5	—	5
Stock based compensation	—	—	—	—	—	—	58	—	58
Net loss	—	—	—	—	—	—	—	(9,611)	(9,611)
Balance at December 31, 2020	6,489,534	$ 12,285	4,000,000	$ 4,000	243,076	$ —	$ 63	$ (13,407)	$ (13,344)

See accompanying notes to financial statements.

AEROVATE THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS
(IN THOUSANDS)

	YEARS ENDED DECEMBER 31,	
	2019	2020
Cash flow from operating activities:		
Net loss	$ (3,330)	$ (9,611)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	—	1
Stock based compensation expense	—	58
Non-cash interest expense	—	75
Change in fair value of convertible promissory notes to related party	—	644
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	2	(103)
Accounts payable	436	37
Accrued and other current liabilities	111	1,040
Net cash used in operating activities	(2,781)	(7,859)
Cash flow from financing activities:		
Proceeds from sale of Series A redeemable convertible preferred stock, net of issuance costs	—	6,413
Proceeds from issuance of convertible promissory notes to related party	—	2,500
Proceeds from exercise of stock options	—	5
Proceeds from issuance of convertible promissory notes to related party	2,500	—
Net cash provided by financing activities	2,500	8,918
Net (decrease) increase in cash	(281)	1,059
Cash at the beginning of the year	3,795	3,514
Cash at the end of the year	$ 3,514	$ 4,573
Supplemental disclosure of noncash investing and financing activities:		
Conversion of convertible promissory notes to related party to Series A redeemable convertible preferred stock	$ —	$ (3,219)
Conversion of convertible promissory notes to related party to Series A redeemable convertible preferred stock	$ —	$ (2,500)
Accrued but unpaid property and equipment purchases	$ —	$ 40

See accompanying notes to financial statements.

AEROVATE THERAPEUTICS, INC.

NOTES TO FINANCIAL STATEMENTS

(1) ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

(a) Organization and Nature of Operations

Aerovate Therapeutics Inc. ("Aerovate" or the "Company") was incorporated in the state of Delaware in July 2018 and is headquartered in Boston, Massachusetts. The Company is a biotechnology company that is focused on the development of AV-101, a novel treatment for pulmonary arterial hypertension ("PAH"). The Company anticipates initiating a Phase 2b/3 trial of AV-101 in PAH patients in the second half of 2021.

(b) Basis of Presentation

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP).

(c) Reverse Stock Split

On June 22, 2021, the Company effected a 1-for-3.1060103 reverse stock split (the "Reverse Stock Split") of its issued and outstanding common stock. Accordingly, the conversion ratio for the Company's outstanding convertible preferred stock was proportionately adjusted such that the common stock issuable upon conversion of such preferred stock was decreased in proportion to the Reverse Stock Split. The par value of the common stock was not adjusted as a result of the Reverse Stock Split. All references to common stock, options to purchase common stock, early exercised options, share data, per share data, convertible preferred stock (to the extent presented on an as-converted to common stock basis) and related information contained in these financial statements have been retrospectively adjusted to reflect the effect of the Reverse Stock Split for all periods presented.

(d) Liquidity and Going Concern

Since inception, the Company has devoted substantially all of its resources to research and development activities, business planning, establishing and maintaining its intellectual property portfolio, hiring personnel, raising capital, and providing general and administrative support for these operations and has not realized revenues from its planned principal operations. The Company has incurred losses and negative cash flows from operations since inception. In addition, the Company expects to incur substantial operating losses for the next several years as it continues its research and development activities. As of December 31, 2020, the Company had cash of $4.6 million.

Given the Company's current operating plan and the uncertainty associated with the achievement or timing of equity, debt financings or other capital resources, Management does not believe it currently has sufficient cash to execute its strategic plan and fund operations beyond twelve months from the issuance date of the financial statements without raising additional funding. As a result, there is substantial doubt about the Company's ability to continue as a going concern. This basis of accounting contemplates the recovery of the Company's assets and the satisfaction of liabilities in the normal course of business and does not include any adjustments to reflect the possible future effects of the recoverability and classification of assets or the amounts and classification of liabilities that might be necessary should the Company be unable to continue as a going concern.

The Company's operations have historically been funded through the sale of preferred stock and convertible notes including the sale of Series Seed redeemable preferred stock during 2018 and the issuance of convertible promissory notes in 2019 (the "2019 Notes"). From July 13, 2020 through August 5, 2020, the Company received aggregate gross proceeds of $9.1 million from the sale of Series A redeemable convertible preferred stock and through the issuance and conversion of $2.5 million of convertible promissory notes issued in July 2020 (the "2020 Notes"). In addition, the Series A Preferred Stock Purchase Agreement ("Stock Purchase Agreement") contains provisions whereby the Company is potentially obligated to sell an additional, aggregate 33,562,620 shares of Series A redeemable convertible preferred stock at $1.893 per share ("Series A Original Issue Price") for aggregate gross proceeds of $63.5 million upon the occurrence of three

defined milestone events ("Milestone Closings") or earlier, at the option of any holder of the Series A redeemable convertible preferred stock.

The Company anticipates achieving the defined milestone funding events and may also look to raise additional or alternative capital through debt or equity financings or other arrangements to fund operations; however, there can be no assurance that the Company will meet the funding milestones or will be able to raise additional or alternative needed capital under acceptable terms, if at all. The sale of additional equity may dilute existing stockholders and newly issued shares may contain senior rights and preferences compared to currently outstanding shares of stock. Issued debt securities may contain covenants and limit the Company's ability to pay dividends or make other distributions to stockholders. If the Company is unable to obtain such additional financing, future operations would need to be scaled back or discontinued.

(e) Use of Estimates

The preparation of the Company's financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that impact the reported amounts of assets, liabilities, expenses, and the disclosure of contingent assets and liabilities in the Company's financial statements and accompanying notes. Accounting estimates and management judgments reflected in the financial statements include: normal recurring accruals, including the accrual of research and development expenses; valuation of deferred tax assets; fair value of convertible promissory notes; fair value of preferred and common stock; and stock-based compensation. Although these estimates are based on the Company's knowledge of current events and actions it may undertake in the future, actual results may materially differ from these estimates and assumptions.

(f) Concentration of Credit Risk

Financial instruments, which potentially subject the Company to concentration of credit risk, consist primarily of cash deposits. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held. The Company has not experienced any losses on deposits since inception.

(g) Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions on how to allocate resources and assess performance. The Company views its operations and manages its business as one operating segment.

(h) Fair Value Option

As permitted under Accounting Standards Codification ("ASC") 825, *Financial Instruments*, ("ASC 825"), the Company has elected the fair value option to account for its convertible promissory notes. In accordance with ASC 825, the Company records these convertible promissory notes at fair value with changes in fair value recorded in the statements of operations. As a result of applying the fair value option, costs related to the issuance of the convertible promissory notes were recognized in earnings as incurred and not deferred.

(i) Fair Value Measurements

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

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Level 1: Observable inputs such as quoted prices in active markets.

Level 2: Inputs, other than the quoted prices in active markets that are observable either directly or indirectly.

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The carrying amounts of the Company's financial instruments, including cash, prepaid expenses, accounts payable, and accrued expenses, approximate fair value due to their short maturities. Convertible promissory notes are classified within the Level 3 designation and are recorded at fair value on a recurring basis. The Company has no financial assets measured at fair value on a recurring basis. None of the Company's non-financial assets or liabilities are recorded at fair value on a non-recurring basis.

As further described in Note 4, on December 30, 2019, the Company issued the 2019 Notes to certain related party investors. The Company elected the fair value option to account for the 2019 Notes and the 2020 Notes. The 2019 Notes and the 2020 Notes were converted into Series A redeemable convertible preferred stock in association with the sale of Series A redeemable convertible preferred stock. There were no convertible promissory notes outstanding as of December 31, 2020.

(j) Cash

As of December 31, 2019 and 2020, the Company had cash balances deposited at major financial institutions and did not have any investments classified as cash equivalents.

(k) Prepaid Expenses and Other Current Assets

Any expenses paid prior to the related services rendered are recorded as prepaid expenses. Such prepaid expenses are expensed in the period the expense is incurred. If the expense is for a service covering multiple periods, it is expensed from the date the services begin and over the period of the service rendered (or contract service period if services rendered dates are not defined).

(l) Property and Equipment, Net

Net property and equipment are stated at historical cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives or the term of the lease, whichever is shorter for the respective assets. Estimated useful lives for research and development equipment is three to five years.

(m) Convertible Preferred Stock

The Company records convertible preferred stock at fair value on the dates of issuance, net of issuance costs. Upon the occurrence of certain events that are outside the Company's control, including a deemed liquidation event, holders of the convertible preferred stock can cause redemption for cash. Therefore, convertible preferred stock is classified outside of stockholders' deficit on the balance sheets as events triggering the liquidation preferences are not solely within the Company's control. The carrying values of the convertible preferred stock are adjusted to their liquidation preferences if and when it becomes probable that such a liquidation event will occur.

(n) Impairment of Long-lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable. The recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset or asset group to the estimated undiscounted future cash flows expected to be generated by the asset or asset group.

If the carrying amount of an asset or asset group exceeds its estimated undiscounted future cash flows, an impairment charge is recognized as the amount by which the carrying amount of the asset or asset group

exceeds the estimated discounted future cash flows of the asset or asset group. There have been no such impairments of long-lived assets for the years ended December 31, 2019 and 2020.

(o) Deferred Offering Costs

The Company capitalizes within other long-term assets certain legal, accounting and other third-party fees that are directly related to the Company's in-process equity financings, including the planned initial public offering, until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds received as a result of the offering. Should a planned equity financing be abandoned, terminated or significantly delayed, the deferred offering costs are immediately written off to operating expenses. The Company did not incur any deferred offering costs as of December 31, 2019 and 2020.

(p) Research and Development Expenses

Research and development expenses are expensed in the periods in which they are incurred. External expenses consist primarily of payments to outside consultants and contract research organizations in connection with the Company's development activities, manufacturing activities, clinical activities, regulatory and other services. External expenses are recognized based on an evaluation of the progress to completion of specific tasks using information provided to the Company by its service providers or the estimate of the level of service that has been performed at each reporting date.

The Company makes estimates of accrued expenses as of each balance sheet date based on facts and circumstances known at that time. The Company periodically confirms the accuracy of its estimates with the service providers and makes adjustments if necessary. The significant estimates in its accrued research and development expenses include the costs incurred for services performed by vendors in connection with research and development activities for which the Company has not yet been invoiced. Research and development expenses amounted to $3.1 million and $7.9 million for the years ended December 31, 2019 and 2020, respectively.

(q) Stock-Based Compensation

The Company recognizes stock-based compensation expense for employee, officer, director and non-employee stock options and restricted stock awards on a straight-line basis over the requisite service period. The Company measures the fair value of stock options at the grant date using the Black-Scholes option-pricing model, which is impacted by the fair value of its common stock, as well as other subjective variables. These variables include, but are not limited to, the expected term of the awards, the expected common stock price volatility over the term of the awards, risk-free interest rates and the expected dividend yield. In accordance with Accounting Standards Update (ASU) 2016-09 *Compensation—Stock Compensation* (Topic 718)—*Improvements to Employee Share Based Payment Accounting*, the Company has elected to recognize the actual forfeitures by reducing the employee stock-based compensation expense in the same period as the forfeitures occur.

The fair value of restricted stock awards is determined on the date of grant based on the estimated fair value of the Company's common stock on that date.

The determination of the fair value of each stock award using the Black-Scholes option-pricing model is affected by the Company's assumptions regarding a number of complex and subjective variables. These variables include, but are not limited to, the fair value of the common stock at the date of grant, the expected term of the awards, the expected stock price volatility over the term of the awards, risk-free interest rate, and dividend rate as follows:

Fair Value of Common Stock. Given the absence of a public trading market, the Company's board of directors considered numerous objective and subjective factors to determine the fair value of the Company's common stock at each grant date. These factors included, but were not limited to: (i) contemporaneous

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third-party valuations of common stock; (ii) the prices for preferred stock sold to outside investors; (iii) the rights and preferences of preferred stock relative to common stock; (iv) the lack of marketability of the Company's common stock; (v) developments in the business; and (vi) the likelihood of achieving a liquidity event, such as an initial public offering ("IPO") or sale of the business, given prevailing market conditions.

Expected Term. The expected term represents the period that the stock-based awards are expected to be outstanding. The Company determines the expected term using the simplified method. The simplified method deems the term to be the average of the time-to-vesting and the contractual life of the options. For stock options granted to non-employees, the expected term equals the remaining contractual term of the option from the vesting date.

Expected Volatility. Given the absence of a public trading market, the expected volatility was estimated by taking the average historic price volatility for industry peers, consisting of several public companies in the Company's industry that are either similar in size, stage, or financial leverage, over a period equivalent to the expected term of the awards.

Risk-Free Interest Rate. The risk-free interest rate is calculated using the average of the published interest rates of U.S. Treasury zero-coupon issues with maturities that are commensurate with the expected term.

Dividend Rate. The dividend yield assumption is zero, as the Company has no plans to make dividend payments.

(r) Common Stock Valuation

Due to the absence of an active market for the Company's common stock, the Company utilized methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants' *Audit and Accounting Practice Guide: Valuation of Privately-Held Company Equity Securities Issued as Compensation* to estimate the fair value of its common stock. In determining the exercise prices for options granted, the Company has considered the fair value of the common stock as of the grant date. The fair value of the common stock has been determined based upon a variety of factors, including the Company's stage of development and material risks related to the business; the progress of the Company's research and development programs, including the status and results of preclinical and clinical studies and progress of the development of manufacturing processes; business conditions and projections; financial position and historical and forecasted performance and operating results; the lack of an active public market for the Company's common stock and preferred stock; the prices of the Company's preferred stock sold to or exchanged between outside investors in arm's length transactions and the rights, preferences, and privileges or preferred stock as compared to those of the Company's common stock, including liquidation preferences of the Company's preferred stock; the analysis of initial public offerings and the market performance of similar companies in the biopharmaceutical industry; the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company in light of prevailing market conditions; the hiring of key personnel and the experience of management; trends and developments in the Company's industry; and external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry.

Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date.

(s) Income Taxes

Income taxes are accounted for using the asset and liability method. Under the asset and liability method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and net operating loss ("NOL") and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences

are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance against deferred tax assets is recorded if, based upon the weight of all available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

(t) Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company's comprehensive loss was the same as its reported net loss for the years ended December 31, 2019 and 2020.

(u) Net Loss Per Share

The two-class method is applicable because the Series A redeemable convertible preferred stock meets the definition of a participating security. Basic net loss per share is calculated by dividing the net loss and increases in the carrying amount of redeemable preferred stock by the weighted-average number of common shares outstanding for the period. Diluted net loss per share is computed by dividing the net loss and increases in the carrying amount of redeemable preferred stock by the weighted average number of common shares and common share equivalents outstanding for the period. Common stock equivalents are only included when their effect is dilutive. The Company's potentially dilutive securities include outstanding stock options under the Company's equity incentive plan and the outstanding convertible preferred stock and have been excluded from the computation of diluted net loss per share as they would be anti-dilutive to the net loss per share. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's net loss position as the inclusion of the potentially dilutive securities would be anti-dilutive.

The following table summarizes the Company's net loss per share:

	YEARS ENDED DECEMBER 31,	
	2019	2020
Numerator:		
Net loss and comprehensive loss	$ (3,330)	$ (9,611)
Accretion of Series A redeemable convertible preferred stock to redemption value	—	(153)
Net loss and comprehensive loss available to common stockholders	$ (3,330)	$ (9,764)
Denominator:		
Weighted-average common stock outstanding, basic and diluted	241,467	242,232
Net loss per share, basic and diluted	$ (13.79)	$ (40.31)

Potentially dilutive securities not included in the calculation of diluted net loss per share attributable to common stockholders because to do so would have had an anti-dilutive effect are as follows (in common stock equivalent shares):

	DECEMBER 31,	
	2019	2020
Series Seed redeemable convertible preferred stock	1,287,825	1,287,825
Series A redeemable convertible preferred stock	—	2,089,341
Common stock options granted and outstanding	—	229,105
Total	1,287,825	3,606,271

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NOTES TO FINANCIAL STATEMENTS

(v) Recently Adopted Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*. ASU 2018-13 considers cost and benefits, and removes, modifies and adds disclosure requirements in Topic 820. The amendments on changes in unrealized gains and losses, the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements, and the narrative description of measurement uncertainty is to be applied prospectively for only the most recent interim or annual period presented in the initial fiscal year of adoption. All other amendments are to be applied retrospectively to all periods presented. ASU 2018-13 is effective for the Company for fiscal years beginning after December 15, 2019, including interim periods within that fiscal year. The adoption of this standard did not have a material impact on the Company's financial statements.

(2) PROPERTY AND EQUIPMENT, NET

Property and equipment, net, consisted of the following (in thousands):

	DECEMBER 31,	
	2019	2020
Research and development equipment	$ —	$ 40
Less accumulated depreciation	—	(1)
Total property and equipment, net	$ —	$ 39

(3) ACCRUED AND OTHER CURRENT LIABILITIES

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

	DECEMBER 31,	
	2019	2020
Accrued research and development	$111	$ 946
Accrued payroll and other employee benefits	—	192
Other	4	18
Total accrued and other current liabilities	$115	$ 1,156

(4) CONVERTIBLE PROMISSORY NOTES

On December 30, 2019, the Company issued convertible promissory notes totaling $2.5 million to RA Capital Healthcare Fund, L.P., Blackwell Partners LLC—Series A, and RA Capital Nexus Fund, L.P. (the "Holders"). The 2019 Notes accrued interest at a rate of 6% per annum and were payable at the demand of the Holders on or after the Maturity Date of December 30, 2021, subject to earlier conversion or repayment in the event of a qualified financing or a change of control, as defined in the convertible promissory notes agreement. Due to certain embedded features, the Company elected to account for the 2019 Notes and all their embedded features under the fair value option. The 2019 Notes were issued at fair value, as such no changes in fair value were recorded between December 30, 2019 and December 31, 2019. The 2019 Notes were converted into Series A redeemable convertible preferred stock in connection with the sale of Series A redeemable convertible preferred stock, with a conversion price of 80% of the Series A Original Issue Price. The Company recorded a change in fair value of $0.6 million for the period January 1, 2020 through conversion on August 5, 2020. In relation to the 2019 Notes, there was no interest expense for the year ended December 31, 2019 and $0.1 million of interest expense for the year ended December 31, 2020.

On July 13, 2020, the Company issued convertible promissory notes totaling $2.5 million to the Holders. The 2020 Notes accrued interest at a rate of 3% per annum and were payable at the demand of the Holders on

or after the Maturity Date of October 31, 2020. The 2020 Notes converted into Series A redeemable convertible preferred stock in association with the sale of Series A redeemable convertible preferred stock on August 5, 2020. The 2020 Notes were issued at fair value and converted at the Series A Original Issue Price, as such no changes in fair value were recorded with respect to the 2020 Notes. In relation to the 2020 Notes, there was no interest expense for the year ended December 31, 2020.

(5) FAIR VALUE OF FINANCIAL INSTRUMENTS

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs (in thousands):

	CONVERTIBLE PROMISSORY NOTES (IN THOUSANDS)
Balance at December 31, 2018	$ —
Issuance of convertible promissory notes, related party	2,500
Balance at December 31, 2019	2,500
Issuance of convertible promissory notes, related party	2,500
Change in fair value of convertible promissory notes, related party	644
Exchange of convertible promissory notes (Note 4)	(5,644)
Balance at December 31, 2020	$ —

(6) STOCKHOLDERS' EQUITY

Under the Amended and Restated Articles of Incorporation dated August 3, 2020, the Company had a total of 94,052,154 shares of capital stock authorized for issuance, consisting of 50,000,000 shares of common stock, par value of $0.0001 per share, and 44,052,154 shares of convertible preferred stock, par value of $0.0001 per share. Shares of authorized convertible preferred stock are designated as 4,000,000 shares of Series Seed redeemable convertible preferred stock and 40,052,154 shares of Series A redeemable convertible preferred stock.

(a) Redeemable Convertible Preferred Stock

In August 2018, the Company sold to RA Capital Health Care Fund, L.P. an aggregate of 4,000,000 shares of Series Seed redeemable preferred stock at a purchase price of $1.00 per share, for net proceeds of $4.0 million. On August 5, 2020, the Company entered into the Stock Purchase Agreement. The Company's initial closing of its Series A redeemable convertible preferred stock occurred on this date. The Company issued 3,468,536 shares of Series A redeemable convertible preferred shares for gross proceeds of $6.6 million at a price per share of $1.893. In addition to the cash proceeds, 3,020,998 shares of Series A redeemable convertible preferred stock were issued in connection with the conversion of the 2019 Notes and the 2020 Notes.

The Stock Purchase Agreement contains provisions that potentially obligate the Company to sell, outside of its control, an additional 33,562,620 shares of Series A redeemable convertible preferred stock at $1.893 per share for expected gross proceeds of $63.5 million, upon the occurrence of three subsequent Milestone Closings or earlier, at the option of any holder of the Series A redeemable convertible preferred stock. If the defined milestones are not achieved prior to the Company's initial public offering, the holders may elect to purchase these shares prior to the completion of the initial public offering. If the shares are not purchased prior to the completion of the initial public offering, then this right to purchase these shares automatically expires.

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Per the terms of the Stock Purchase Agreement the right and obligation to participate in the Milestone Closings is not legally detachable from the ownership of the Series A redeemable convertible preferred stock. Additionally, if any holder of the Series A redeemable convertible preferred stock does not elect to participate in the three subsequent Milestone Closings, the holder's shares of Series A redeemable convertible preferred stock automatically convert into shares of common stock at a ratio of two shares of Series A redeemable convertible preferred stock to one share of common stock. The Company performed an assessment of the Stock Purchase Agreement in accordance with the authoritative guidance and concluded that the rights and obligations associated with the Milestone Closings do not meet the definition of a freestanding financial instrument as they are not legally detachable or transferable and are clearly and closely related to the Series A redeemable convertible preferred shares.

The Company's preferred stock has the following characteristics:

(1) Dividends

Dividends shall be payable only when and if declared by the Company's Board of Directors and shall not be cumulative. The Company shall declare all dividends pro rata on the common stock and preferred stock on a pari passu basis according to the number of shares of common stock held by such holders.

No such dividends have been declared or paid as of December 31, 2020.

(2) Liquidation

The holders of the Series A redeemable convertible preferred stock are entitled to receive liquidation preferences at the original issue price of $1.893, plus all accrued and declared but unpaid dividends. Holders of Series A redeemable convertible preferred stock are entitled to liquidation preferences that have priority and are made in preference to any payments to the holders of the Series Seed redeemable convertible preferred stock and common stock.

After full payment of the liquidation preference to the holders of the Series A redeemable convertible preferred stock, the remaining assets, if any, will be distributed to the holders of the Series Seed redeemable convertible preferred stock at the Series Seed original issue price of $1.00, plus all accrued and declared but unpaid dividends. The Series Seed redeemable convertible preferred stock shall be entitled to receive upon such liquidation the greater of (i) the amount distributed pursuant to above and (ii) the amount such holder would have received if all shares of Series Seed redeemable convertible preferred stock had been converted into common stock immediately prior to such liquidation.

After full payment of the liquidation preference to the holders of the Series Seed redeemable convertible preferred stock, the remaining assets, if any, will be distributed ratably to the holders of the Series A redeemable convertible preferred stock and common stock pro rata based on the number of shares held by each holder, treating for this purpose all such securities as if they had been converted to common stock immediately prior to such liquidation; provided, however that the aggregate amount which the holders of Series A redeemable convertible preferred stock shall be entitled to receive shall be the greater of $5.679 per share and the amount the holder would have received if all shares of Series A redeemable convertible preferred stock had been converted into common stock immediately prior to such liquidation.

(3) Conversion Rights

The shares of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock are convertible into an equal number of shares of common stock, at the option of the holder, subject to certain anti-dilution adjustments. The conversion rate for the convertible preferred stock is determined by dividing the original issue price, as adjusted for stock splits, by the conversion price. The conversion price is initially the original issue prices, but is subject to adjustment for dividends, stock splits, and other distributions. The conversion rate at December 31, 2020 for the Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock was 1:1. Upon the effective date of the Reverse Stock Split, the conversion rate was adjusted to 1:0.3220.

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NOTES TO FINANCIAL STATEMENTS

Each share of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock are automatically converted into common stock at the then effective conversion rate (i) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock for the account of the Company in which the price per share of common stock is at least three times the Series A Original Issue Price and the gross cash proceeds to the Company are at least $50.0 million or (ii) upon the vote or written consent for such conversion from the Requisite Holders (defined as at least 65% of the holders of Series A redeemable convertible preferred stock).

(4) Redemption Rights

The holders of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock have redemption rights. Any time on or after the fifth anniversary of the most recent closing conducted in accordance with the Series A redeemable convertible preferred stock, the Requisite Holders may provide written notice requesting redemption of all shares of convertible preferred stock at a price equal to the original issue price, plus all declared but unpaid dividends. The redemption shall be paid in three annual installments commencing not more than sixty days after the written notice.

(5) Voting

The holder of each share of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock are entitled to one vote for each share of common stock into which it would convert and to vote as one class with the common stockholders on all matters.

(b) Common Stock

In August 2018, the Company issued 241,467 shares of common stock to RA Capital Healthcare Fund, L.P. at a price of $0.0012 per share.

The voting, dividend, and liquidation rights of the holders of the common stock are subject to, and qualified by, the rights, powers, and preferences of the holders of the preferred stock. The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of stockholders.

Common stock reserved for future issuance consisted of the following:

	DECEMBER 31,	
	2019	2020
Series Seed redeemable convertible preferred stock	1,287,825	1,287,825
Series A redeemable convertible preferred stock	—	2,089,341
Common stock options granted and outstanding	—	229,105
Common stock reserved for future option grants	80,489	171,285
Total	1,368,314	3,777,556

(7) SHARE-BASED COMPENSATION

(a) Stock Option Plan

In August 2018, the Company adopted the 2018 Equity Incentive Plan (the “Plan”), which allowed for the issuance of incentive stock options (“ISOs”), nonstatutory stock options (“NSOs”), and restricted stock units. The Plan was established to enable the Company to attract and retain personnel, to provide additional incentive to its employees, directors, and consultants of the Company and to promote the financial success and progress of the Company. Under the Plan, the Company can offer ISOs to employees and NSOs to employees, non-employee directors, and consultants. The Plan allows the Company to issue options for shares of its

AEROVATE THERAPEUTICS, INC.

NOTES TO FINANCIAL STATEMENTS

common stock up to a total of 401,999 shares (the "Option Pool"), subject to appropriate adjustments for stock splits, combinations and other similar events for issuance pursuant to awards made under the Plan.

The options that are granted under the Plan are exercisable at various dates as determined upon grant and terminate within 10 years of the date of grant. The vesting period generally occurs over three to four years.

Stock option activity under the Plan, is as follows:

	OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE	WEIGHTED-AVERAGE REMAINING CONTRACTUAL TERM (IN YEARS)	AGGREGATE INTRINSIC VALUE (IN THOUSANDS)
Outstanding at December 31, 2019	—	$ —	—	$ —
Granted	230,714	1.74		
Exercised	(1,609)	2.95		
Cancelled/Forfeited	—	—		
Outstanding at December 31, 2020	229,105	$ 1.74	9.69	$ —
Vested and exercisable at December 31, 2020	8,704	$ 1.74	9.68	$ —
Vested and expected to vest at December 31, 2020	229,105	$ 1.74	9.69	$ —

All exercisable options are vested and all outstanding options are vested or expected to vest.

The total intrinsic value of options exercised during the year ended December 31, 2019 and 2020 was $0.0 million. The intrinsic value is the difference between the estimated fair value of the Company's common stock at the time of exercise, as determined by the board of directors, and the exercise price of the stock option.

The Company estimated the fair value of stock options using the Black-Scholes valuation model. The Company accounts for any forfeitures of options when they occur. Previously recognized compensation expense for an award is reversed in the period that the award is forfeited. The fair value of stock options was estimated using the following assumptions:

	YEARS ENDED DECEMBER 31,	
	2019	2020
Expected term (in years)	—	5.5 – 6.1
Expected volatility	—	68.0 – 79.4%
Risk-free interest rate	—	0.4 – 1.5%
Expected dividend	—	—

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NOTES TO FINANCIAL STATEMENTS

Stock-based compensation expense recognized for stock option grants has been reported in the statements of operations and comprehensive loss as follows (in thousands):

	YEARS ENDED DECEMBER 31,	
	2019	2020
Research and development	$ —	$ 30
General and administrative	—	28
Total	$ —	$ 58

As of December 31, 2020, there was approximately $0.3 million of total unrecognized stock-based compensation expense related to nonvested stock-based compensation arrangements granted under the Plan, which is expected to be recognized over a weighted-average period of approximately 3.2 years.

(8) RELATED PARTY TRANSACTIONS

Services Agreement

In August 2018, the Company entered into a services agreement ("Services Agreement") with Carnot, LLC ("Carnot"), an entity owned and controlled by RA Capital Management, L.P. under which Carnot provides research and other services to the Company. RA Capital Management, L.P. is a related party due to its equity ownership of the Company. The Company pays Carnot for services performed and costs incurred. The Services Agreement is for a term of two years. The Company may terminate the Services Agreement by giving 30 days' prior notice and either party can terminate the services agreement for a material breach, if not cured within 30 days following notice by the nonbreaching party.

In July 2019, the Services Agreement with Carnot was amended whereby research and other services are now performed by Carnot Pharma, LLC ("Carnot Pharma"), an entity owned and controlled by RA Capital Management, L.P., and the term was updated to the later of (i) two years from July 15, 2019 and (ii) completion of services under the agreement.

Expenses incurred by the Company under the Services Agreement with Carnot Pharma totaled $20,335 and $0.1 million for the years ended December 31, 2019 and 2020, respectively, and are presented in the statement of operations and comprehensive loss as research and development and general and administrative expenses. As of December 31, 2019 and December 31, 2020, $3,117 and $5,632, respectively, was due to Carnot Pharma, LLC by the Company for services rendered under the agreement.

(9) INCOME TAXES

Significant components of the Company's net deferred tax assets are as follows (in thousands):

	DECEMBER 31,	
	2019	2020
Deferred income tax assets:		
NOL and credit carryforwards	$ 990	$ 2,836
Compensation accruals	—	38
Intangible assets	1	9
Other	—	2
Gross deferred tax assets	991	2,885
Less: valuation allowance	(991)	(2,885)
Total deferred tax assets	—	—
Net deferred tax assets	$ —	$ —

AEROVATE THERAPEUTICS, INC.

NOTES TO FINANCIAL STATEMENTS

A reconciliation between the provision for income taxes and income taxes computed using the U.S. federal statutory corporate tax rate is as follows (in thousands):

	YEARS ENDED DECEMBER 31,	
	2019	2020
Income taxes computed at the statutory rate	$ (699)	$ (2,018)
State taxes	(210)	(89)
Permanent differences	11	41
Convertible promissory notes	—	151
Stock-based compensation	—	10
Other	—	11
Change in valuation allowance	899	1,894
Total tax provision	$ 1	$ —

The Company had federal NOL carryforwards available of $3.6 million and $12.0 million as of December 31, 2019 and 2020, respectively, before consideration limitations under Section 382 of the Internal Revenue Code or Section 382, as further described below. The NOL generated from 2018 onwards of $12.0 million will carryforward indefinitely and be available to offset up to 80% of future taxable income each year. Additionally, the Company had state NOL carryforwards available of $3.6 million and $7.3 million as of December 31, 2019 and 2020, respectively. The state NOLs may be used to offset future taxable income and will begin to expire in 2034. Additionally, the Company had federal and state research and development credit carryforwards available of $6,896 and $0.1 million as of December 31, 2019 and 2020 that will begin to expire in 2038.

The future utilization of the Company's NOL and tax credit carryforwards to offset future taxable income may be subject to a substantial annual limitation as a result of changes in ownership by stockholders that hold 5% or more of the Company's common stock. An assessment of such ownership changes under Section 382 and 383 was not completed through December 31, 2020. To the extent that an assessment is completed in the future, the Company's ability to utilize tax attributes could be restricted on a year-by-year basis and certain attributes could expire before they are utilized. The Company will examine the impact of any potential ownership changes in the future.

The Company has established a full valuation allowance for its deferred tax assets due to uncertainties that preclude it from determining that it is more likely than not that the Company will be able to generate sufficient taxable income to realize such assets. Management assesses the available positive and negative evidence to estimate if sufficient future taxable income will be generated to utilize the existing deferred tax assets. A significant piece of objective negative evidence evaluated was the cumulative loss incurred since inception. Such objective evidence limits the ability to consider other subjective evidence such as the Company's projections for future growth. Based on this evaluation, as of December 31, 2019 and 2020, a valuation allowance of $1.0 million and $2.9 million, respectively, has been recorded against all of the Company's net deferred tax assets, as the Company has determined that none of the Company's balance of net deferred tax assets is more likely than not to be realized. The amount of the deferred tax assets considered realizable, however, could be adjusted in the future if objective negative evidence in the form of cumulative losses is no longer present and additional weight may be given to subjective evidence, such as estimates of future taxable income during carryforward periods and the Company's projections for growth.

The Company is subject to taxation in the United States, California and Massachusetts. The Company's Federal and state returns are subject to examination, as 2018 was the first year of operations for the Company.

(10) COMMITMENTS AND CONTINGENCIES

From time to time, the Company may become subject to claims or suits arising in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will

be made and such expenditures can be reasonably estimated. As of December 31, 2019 and 2020, the Company is not a party to any litigation and has not recorded any such liabilities.

(11) SUBSEQUENT EVENTS

The Company has evaluated subsequent events from the balance sheet date through May 6, 2021, the date the financial statements were available to be issued, except for the 1-for-3.1060103 reverse stock split discussed in Note 1 which was effective as of June 22, 2021.

On February 1, 2021, upon the completion of the first of three defined milestone closings (the "First Milestone Closing") outlined in the Stock Purchase Agreement, the Company sold 4,224,274 shares of Series A redeemable convertible preferred stock at $1.893 per share for aggregate gross proceeds of $8.0 million.

In April 2021, the Company granted an aggregate of 1,701,540 ISOs and NSOs to certain of its employees and nonemployees under the Plan, each with an exercise price of $2.14 per share.

AEROVATE THERAPEUTICS, INC.

CONDENSED BALANCE SHEETS
(UNAUDITED)
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	DECEMBER 31, 2020 (NOTE 1)	MARCH 31, 2021
Assets		
Current assets:		
Cash	$ 4,573	$ 8,641
Prepaid expenses and other current assets	103	963
Total current assets	4,676	9,604
Property and equipment, net (Note 2)	39	37
Other long-term assets	—	307
Total assets	$ 4,715	$ 9,948
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable (including related party amounts of $18 and $9, respectively)	$ 618	$ 1,550
Accrued and other current liabilities (Note 3)	1,156	232
Total current liabilities	1,774	1,782
Commitments and contingencies (Note 9)		
Series A redeemable convertible preferred stock, $0.0001 par value; 40,052,154 shares authorized at December 31, 2020 and March 31, 2021; 6,489,534 and 10,713,808 shares issued and outstanding at December 31, 2020 and March 31, 2021, respectively; aggregate liquidation preference of $20,281 at March 31, 2021	12,285	20,281
Series Seed redeemable convertible preferred stock, $0.0001 par value; 4,000,000 shares authorized, issued and outstanding at December 31, 2020 and March 31, 2021; aggregate liquidation preference of $4,000 at March 31, 2021	4,000	4,000
Stockholders' deficit:		
Common stock, $0.0001 par value; 50,000,000 shares authorized at December 31, 2020 and March 31, 2021; 243,076 shares issued and outstanding at December 31, 2020 and March 31, 2021	—	—
Additional paid-in capital	63	86
Accumulated deficit	(13,407)	(16,201)
Total stockholders' deficit	(13,344)	(16,115)
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	$ 4,715	$ 9,948

See accompanying notes to unaudited interim condensed financial statements.

AEROVATE THERAPEUTICS, INC.

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	THREE MONTHS ENDED MARCH 31,	
	2020	2021
Operating expenses:		
Research and development (includes related party amounts of $16 and $15, respectively)	$ 1,206	$ 2,196
General and administrative (includes related party amounts of $8 and $5, respectively)	152	584
Total operating expenses	1,358	2,780
Loss from operations	(1,358)	(2,780)
Other expense:		
Interest expense	(38)	—
Change in fair value of convertible promissory notes	(40)	—
Other expense	—	(1)
Total other expense	(78)	(1)
Net loss and comprehensive loss	$ (1,436)	$ (2,781)
Net loss per share, basic and diluted	$ (5.95)	$ (11.49)
Weighted-average shares of common stock outstanding, basic and diluted	241,467	243,076

See accompanying notes to unaudited interim condensed financial statements.

AEROVATE THERAPEUTICS, INC.

CONDENSED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
(UNAUDITED)
(IN THOUSANDS, EXCEPT SHARE AMOUNTS)

	SERIES A REDEEMABLE CONVERTIBLE PREFERRED STOCK		SERIES SEED REDEEMABLE CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDERS' DEFICIT
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT			
Balance at December 31, 2019	—	—	4,000,000	4,000	241,467	—	—	(3,643)	(3,643)
Stock based compensation	—	—	—	—	—	—	7	—	7
Net loss	—	—	—	—	—	—	—	(1,436)	(1,436)
Balance at March 31, 2020	—	$ —	4,000,000	$ 4,000	241,467	$ —	$ 7	$ (5,079)	$ (5,072)

	SERIES A REDEEMABLE CONVERTIBLE PREFERRED STOCK		SERIES SEED REDEEMABLE CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED DEFICIT	TOTAL STOCKHOLDEI DEFICIT
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT			
Balance at December 31, 2020	6,489,534	12,285	4,000,000	4,000	243,076	—	63	(13,407)	(13,34
Issuance of Series A redeemable convertible preferred stock at $1.893 per share, net of issuance costs of $13	4,224,274	7,983	—	—	—	—	—	—	–
Accretion of Series A redeemable convertible preferred stock to redemption value	—	13	—	—	—	—	—	(13)	(1
Stock based compensation	—	—	—	—	—	—	23	—	2
Net loss	—	—	—	—	—	—	—	(2,781)	(2,78
Balance at March 31, 2021	10,713,808	$ 20,281	4,000,000	$ 4,000	243,076	$ —	$ 86	$ (16,201)	$ (16,11

See accompanying notes to unaudited interim condensed financial statements.

AEROVATE THERAPEUTICS, INC.

CONDENSED STATEMENTS OF CASH FLOWS
(UNAUDITED)
(IN THOUSANDS)

	THREE MONTHS ENDED MARCH 31,	
	2020	2021
Cash flow from operating activities:		
Net loss	$(1,436)	$ (2,781)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	—	2
Stock based compensation expense	7	23
Non-cash interest expense	38	—
Change in fair value of convertible promissory notes to related party	40	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(74)	(860)
Accounts payable	91	765
Accrued and other current liabilities	151	(924)
Net cash used in operating activities	(1,183)	(3,775)
Cash flow from investing activities:		
Purchases of property and equipment	—	(40)
Net cash used in investing activities	—	(40)
Cash flow from financing activities:		
Proceeds from sale of Series A redeemable convertible preferred stock, net of issuance costs	—	7,983
Payments for deferred offering costs	—	(100)
Net cash provided by financing activities	—	7,883
Net (decrease) increase in cash	(1,183)	4,068
Cash at the beginning of the year	3,514	4,573
Cash at the end of the period	$ 2,331	$ 8,641
Supplemental disclosure of noncash investing and financing activities:		
Deferred offering costs included in accounts payable	$ —	$ 207

See accompanying notes to unaudited interim condensed financial statements.

AEROVATE THERAPEUTICS, INC.

NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

(1) Organization and Summary of Significant Accounting Policies

(a) Organization and Nature of Operations

Aerovate Therapeutics Inc. ("Aerovate" or the "Company") was incorporated in the state of Delaware in July 2018 and is headquartered in Boston, Massachusetts. The Company is a biotechnology company that is focused on the development of AV-101, a novel treatment for pulmonary arterial hypertension ("PAH"). The Company anticipates initiating a Phase 2b/3 trial of AV-101 in PAH patients in the second half of 2021.

(b) Basis of Presentation

The accompanying unaudited condensed financial statements as of March 31, 2021 and for the three months ended March 31, 2020 and 2021 have been prepared in conformity with generally accepted accounting principles ("GAAP") in the United States of America for interim financial information and pursuant to Article 10 of Regulation S-X of the Securities Act of 1933, as amended (the Securities Act). Accordingly, they do not include all of the information and notes required by GAAP for complete financial statements. These unaudited condensed financial statements include only normal and recurring adjustments that the Company believes are necessary to fairly state the Company's financial position and the results of its operations and cash flows. The results for the three months ended March 31, 2021 are not necessarily indicative of the results expected for the full fiscal year or any subsequent interim period. The condensed balance sheet as of December 31, 2020 has been derived from the audited financial statements at that date but does not include all disclosures required by GAAP for complete financial statements. Because all of the disclosures required by GAAP for complete financial statements are not included herein, these unaudited condensed financial statements and the notes accompanying them should be read in conjunction with the Company's audited financial statements as of and for the year ended December 31, 2020. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB").

(c) Reverse Stock Split

On June 22, 2021, the Company effected a 1-for-3.1060103 reverse stock split (the "Reverse Stock Split") of its issued and outstanding common stock. Accordingly, the conversion ratio for the Company's outstanding convertible preferred stock was proportionately adjusted such that the common stock issuable upon conversion of such preferred stock was decreased in proportion to the Reverse Stock Split. The par value of the common stock was not adjusted as a result of the Reverse Stock Split. All references to common stock, options to purchase common stock, early exercised options, share data, per share data, convertible preferred stock (to the extent presented on an as-converted to common stock basis) and related information contained in these financial statements have been retrospectively adjusted to reflect the effect of the Reverse Stock Split for all periods presented.

(d) Liquidity and Going Concern

Since inception, the Company has devoted substantially all of its resources to research and development activities, business planning, establishing and maintaining its intellectual property portfolio, hiring personnel, raising capital, and providing general and administrative support for these operations and has not realized revenues from its planned principal operations. The Company has incurred losses and negative cash flows from operations since inception. In addition, the Company expects to incur substantial operating losses for the next several years as it continues its research and development activities. As of March 31, 2021, the Company had cash of $8.6 million.

The Company's operations have historically been funded through the sale of preferred stock and convertible notes including the sale of Series Seed redeemable convertible preferred stock during 2018 and the issuance of convertible promissory notes in 2019 (the "2019 Notes"), which resulted in aggregate gross proceeds of $4.0 million and $2.5 million, respectively. From July 13, 2020 through August 5, 2020, the Company received aggregate gross proceeds of $9.1 million from the sale of Series A redeemable convertible preferred stock and through the issuance and conversion of $2.5 million of convertible promissory notes issued in

July 2020 (the "2020 Notes"). On February 1, 2021, upon the completion of the first of three defined milestone closings ("First Milestone Closing") outlined in the Series A Preferred Stock Purchase Agreement ("Stock Purchase Agreement"), the Company received aggregate gross proceeds of $8.0 million from the sale of Series A redeemable convertible preferred stock at $1.893 per share ("Series A Original Issue Price"). As described in Note 10, on June 4, 2021, upon the completion of the second milestone closing ("Second Milestone Closing") and the third milestone closing ("Third Milestone Closing") outlined in the Stock Purchase Agreement, the Company received aggregate gross proceeds of $55.5 million from the sale of Series A redeemable convertible preferred stock at the Series A Original Issue Price.

After considering the additional proceeds received on June 4, 2021 in addition to its existing cash on-hand, Management has concluded that the Company will have sufficient working capital on-hand to fund operations for at least 12 months from the date that these unaudited condensed financial statements are issued. Management expects operating losses to continue for the foreseeable future and the Company will need to raise additional capital. If the Company is unable to obtain such additional financing, future operations would need to be scaled back or discontinued.

(e) Deferred Offering Costs

The Company capitalizes within other long-term assets certain legal, accounting and other third-party fees that are directly related to the Company's in-process equity financings, including the planned initial public offering, until such financings are consummated. After consummation of the equity financing, these costs are recorded as a reduction of the proceeds received as a result of the offering. Should a planned equity financing be abandoned, terminated or significantly delayed, the deferred offering costs are immediately written off to operating expenses. As of December 31, 2020 and March 31, 2021, deferred offering costs of $0.0 million and $0.3 million, respectively, were recorded within other long-term assets on the balance sheet.

(f) Net Loss Per Share

The two-class method is applicable because the Series A redeemable convertible preferred stock meets the definition of a participating security. Basic net loss per share is calculated by dividing the net loss and increases in the carrying amount of redeemable preferred stock by the weighted-average number of common shares outstanding for the period. Diluted net loss per share is computed by dividing the net loss and increases in the carrying amount of redeemable preferred stock by the weighted average number of common shares and common share equivalents outstanding for the period. Common stock equivalents are only included when their effect is dilutive. The Company's potentially dilutive securities include outstanding stock options under the Company's equity incentive plan and the outstanding convertible preferred stock and have been excluded from the computation of diluted net loss per share as they would be anti-dilutive to the net loss per share. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's net loss position as the inclusion of the potentially dilutive securities would be anti-dilutive.

AEROVATE THERAPEUTICS, INC.

NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

The following table summarizes the Company's net loss per share (in thousands, except share and per share amounts):

	THREE MONTHS ENDED MARCH 31,	
	2020	2021
Numerator:		
Net loss and comprehensive loss	$ (1,436)	$ (2,781)
Accretion of Series A redeemable convertible preferred stock to redemption value	—	(13)
Net loss and comprehensive loss available to common stockholders	$ (1,436)	$ (2,794)
Denominator:		
Weighted-average common stock outstanding, basic and diluted	241,467	243,076
Net loss per share, basic and diluted	$ (5.95)	$ (11.49)

Potentially dilutive securities not included in the calculation of diluted net loss per share attributable to common stockholders because to do so would have had an anti-dilutive effect are as follows (in common stock equivalent shares):

	DECEMBER 31, 2020	MARCH 31, 2021
Series Seed redeemable convertible preferred stock	1,287,825	1,287,825
Series A redeemable convertible preferred stock	2,089,341	3,449,369
Options to purchase common stock	229,105	229,105
Total	3,606,271	4,966,299

(2) Property and Equipment, Net

Property and equipment, net, consisted of the following (in thousands):

	DECEMBER 31, 2020	MARCH 31, 2021
Research and development equipment	$ 40	$ 40
Less accumulated depreciation	(1)	(3)
Total property and equipment, net	$ 39	$ 37

(3) Accrued and Other Current Liabilities

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

	DECEMBER 31, 2020	MARCH 31, 2021
Accrued research and development	$ 946	$ 104
Accrued payroll and other employee benefits	192	96
Other	18	32
Total accrued and other current liabilities	$ 1,156	$ 232

AEROVATE THERAPEUTICS, INC.

NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

(4) Convertible Promissory Notes

On December 30, 2019, the Company issued convertible promissory notes totaling $2.5 million to RA Capital Healthcare Fund, L.P., Blackwell Partners LLC — Series A, and RA Capital Nexus Fund, L.P. (the "Holders"). The 2019 Notes accrued interest at a rate of 6% per annum and were payable at the demand of the Holders on or after the Maturity Date of December 30, 2021, subject to earlier conversion or repayment in the event of a qualified financing or a change of control, as defined in the convertible promissory notes agreement. Due to certain embedded features, the Company elected to account for the 2019 Notes and all their embedded features under the fair value option. The 2019 Notes were issued at fair value, as such no changes in fair value were recorded between December 30, 2019 and December 31, 2019. The 2019 Notes were converted into Series A redeemable convertible preferred stock in connection with the initial closing of Series A redeemable convertible preferred stock on August 5, 2020, with a conversion price of 80% of the Series A Original Issue Price. The Company recorded a change in fair value of $0.6 million for the period January 1, 2020 through conversion on August 5, 2020. In relation to the 2019 Notes, there was $37,999 of interest expense for the three months ended March 31, 2020.

On July 13, 2020, the Company issued convertible promissory notes totaling $2.5 million to the Holders. The 2020 Notes accrued interest at a rate of 3% per annum and were payable at the demand of the Holders on or after the Maturity Date of October 31, 2020. The 2020 Notes converted into Series A redeemable convertible preferred stock in association with the initial closing of Series A redeemable convertible preferred stock on August 5, 2020. The 2020 Notes were issued at fair value and converted at the Series A Original Issue Price, as such no changes in fair value were recorded with respect to the 2020 Notes.

(5) Fair Value of Financial Instruments

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs (in thousands):

	CONVERTIBLE PROMISSORY NOTES (IN THOUSANDS)
Balance at December 31, 2019	$ 2,500
Change in fair value of convertible promissory notes, related party	40
Balance at March 31, 2020	$ 2,540

There are no liabilities measured at fair value for the three months ended March 31, 2021.

(6) Stockholders' Equity

Under the Amended and Restated Articles of Incorporation dated August 3, 2020, the Company had a total of 94,052,154 shares of capital stock authorized for issuance, consisting of 50,000,000 shares of common stock, par value of $0.0001 per share, and 44,052,154 shares of convertible preferred stock, par value of $0.0001 per share. Shares of authorized convertible preferred stock are designated as 4,000,000 shares of Series Seed redeemable convertible preferred stock and 40,052,154 shares of Series A redeemable convertible preferred stock.

(a) Redeemable Convertible Preferred Stock

In August 2018, the Company sold to RA Capital Health Care Fund, L.P. an aggregate of 4,000,000 shares of Series Seed redeemable preferred stock at a purchase price of $1.00 per share, for net proceeds of $4.0 million. On August 5, 2020, the Company entered into the Stock Purchase Agreement. The Company's initial closing of its Series A redeemable convertible preferred stock occurred on this date. The Company issued 3,468,536 shares of Series A redeemable convertible preferred shares for gross proceeds of $6.6 million at

a price per share of $1.893. In addition to the cash proceeds, 3,020,998 shares of Series A redeemable convertible preferred stock were issued in connection with the conversion of the 2019 Notes and the 2020 Notes.

The Stock Purchase Agreement contained provisions that potentially obligated the Company to sell, outside of its control, an additional 33,562,620 shares of Series A redeemable convertible preferred stock at $1.893 per share for expected gross proceeds of $63.5 million, upon the occurrence of three subsequent Milestone Closings or earlier, at the option of any holder of the Series A redeemable convertible preferred stock. If the defined milestones were not achieved prior to the Company's initial public offering, the holders had the right to purchase these shares prior to the completion of the initial public offering. If the shares were not purchased prior to the completion of the initial public offering, then this right to purchase these shares would have automatically expired.

On February 1, 2021, upon the completion of the First Milestone Closing, the Company sold 4,224,274 shares of Series A redeemable convertible preferred stock at the Series A Original Issue Price for aggregate gross proceeds of $8.0 million. On June 4, 2021, upon the completion of the Second Milestone Closing and the Third Milestone Closing, the Company sold 29,338,346 shares of Series A redeemable convertible preferred stock at the Series A Original Issue Price for aggregate gross proceeds of $55.5 million.

The Company's preferred stock has the following characteristics:

(1) Dividends

Dividends shall be payable only when and if declared by the Company's Board of Directors and shall not be cumulative. The Company shall declare all dividends pro rata on the common stock and preferred stock on a pari passu basis according to the number of shares of common stock held by such holders.

No such dividends have been declared or paid as of March 31, 2021.

(2) Liquidation

The holders of the Series A redeemable convertible preferred stock are entitled to receive liquidation preferences at the original issue price of $1.893, plus all accrued and declared but unpaid dividends. Holders of Series A redeemable convertible preferred stock are entitled to liquidation preferences that have priority and are made in preference to any payments to the holders of the Series Seed redeemable convertible preferred stock and common stock.

After full payment of the liquidation preference to the holders of the Series A redeemable convertible preferred stock, the remaining assets, if any, will be distributed to the holders of the Series Seed redeemable convertible preferred stock at the Series Seed original issue price of $1.00, plus all accrued and declared but unpaid dividends. The Series Seed redeemable convertible preferred stock shall be entitled to receive upon such liquidation the greater of (i) the amount distributed pursuant to above and (ii) the amount such holder would have received if all shares of Series Seed redeemable convertible preferred stock had been converted into common stock immediately prior to such liquidation.

After full payment of the liquidation preference to the holders of the Series Seed redeemable convertible preferred stock, the remaining assets, if any, will be distributed ratably to the holders of the Series A redeemable convertible preferred stock and common stock pro rata based on the number of shares held by each holder, treating for this purpose all such securities as if they had been converted to common stock immediately prior to such liquidation; provided, however that the aggregate amount which the holders of Series A Series A redeemable convertible preferred stock shall be entitled to receive shall be the greater of $5.679 per share and the amount the holder would have received if all shares of Series A redeemable convertible preferred stock had been converted into common stock immediately prior to such liquidation.

AEROVATE THERAPEUTICS, INC.

NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

(3) Conversion Rights

The shares of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock are convertible into an equal number of shares of common stock, at the option of the holder, subject to certain anti-dilution adjustments. The conversion rate for the convertible preferred stock is determined by dividing the original issue price, as adjusted for stock splits, by the conversion price. The conversion price is initially the original issue prices, but is subject to adjustment for dividends, stock splits, and other distributions. The conversion rate at March 31, 2021 for the Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock was 1:1. Upon the effective date of the Reverse Stock Split, the conversion rate was adjusted to 1:0.3220.

Each share of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock are automatically converted into common stock at the then effective conversion rate (i) immediately upon the closing of a firmly underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, covering the offer and sale of common stock for the account of the Company in which the price per share of common stock is at least three times the Series A Original Issue Price and the gross cash proceeds to the Company are at least $50.0 million or (ii) upon the vote or written consent for such conversion from the Requisite Holders (defined as at least 65% of the holders of Series A redeemable convertible preferred stock).

(4) Redemption Rights

The holders of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock have redemption rights. Any time on or after the fifth anniversary of the most recent closing conducted in accordance with the Series A redeemable convertible preferred stock, the Requisite Holders may provide written notice requesting redemption of all shares of convertible preferred stock at a price equal to the original issue price, plus all declared but unpaid dividends. The redemption shall be paid in three annual installments commencing not more than sixty days after the written notice.

(5) Voting

The holder of each share of Series A redeemable convertible preferred stock and Series Seed redeemable convertible preferred stock are entitled to one vote for each share of common stock into which it would convert and to vote as one class with the common stockholders on all matters.

(b) Common Stock

In August 2018, the Company issued 241,467 shares of common stock to RA Capital Healthcare Fund, L.P. at a price of $0.0012 per share.

The voting, dividend, and liquidation rights of the holders of the common stock are subject to, and qualified by, the rights, powers, and preferences of the holders of the preferred stock. The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of stockholders.

Common stock reserved for future issuance consisted of the following:

	DECEMBER 31, 2020	MARCH 31, 2021
Series Seed redeemable convertible preferred stock	1,287,825	1,287,825
Series A redeemable convertible preferred stock	2,089,341	3,449,369
Common stock options granted and outstanding	229,105	229,105
Common stock reserved for future option grants	171,285	171,285
Total	3,777,556	5,137,584

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(7) Share-Based Compensation

(a) Stock Option Plan

In August 2018, the Company adopted the 2018 Equity Incentive Plan (the "Plan"), which allowed for the issuance of incentive stock options ("ISOs"), nonstatutory stock options ("NSOs"), and restricted stock units. The Plan was established to enable the Company to attract and retain personnel, to provide additional incentive to its employees, directors, and consultants of the Company and to promote the financial success and progress of the Company. Under the Plan, the Company can offer ISOs to employees and NSOs to employees, non-employee directors, and consultants. The Plan allows the Company to issue options for shares of its common stock up to a total of 401,999 shares (the "Option Pool"), subject to appropriate adjustments for stock splits, combinations and other similar events for issuance pursuant to awards made under the Plan.

The options that are granted under the Plan are exercisable at various dates as determined upon grant and terminate within 10 years of the date of grant. The vesting period generally occurs over three to four years.

Stock option activity under the Plan, is as follows:

	OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE	WEIGHTED- AVERAGE REMAINING CONTRACTUAL TERM (IN YEARS)	AGGREGATE INTRINSIC VALUE (IN THOUSANDS)
Outstanding at December 31, 2020	229,105	$ 1.74	9.69	$ —
Granted	—	—		
Exercised	—	—		
Cancelled/Forfeited	—	—		
Outstanding at March 31, 2021	229,105	$ 1.74	9.44	$ —
Vested and exercisable at March 31, 2021	21,663	$ 1.74	9.43	$ —
Vested and expected to vest at March 31, 2021	229,105	$ 1.74	9.44	$ —

All exercisable options are vested and all outstanding options are vested or expected to vest.

The total intrinsic value of options exercised during the three months ended March 31, 2021 was $0.0 million. The intrinsic value is the difference between the estimated fair value of the Company's common stock at the time of exercise, as determined by the board of directors, and the exercise price of the stock option.

The Company estimated the fair value of stock options using the Black-Scholes valuation model. The Company accounts for any forfeitures of options when they occur. Previously recognized compensation expense for an award is reversed in the period that the award is forfeited. The fair value of stock options was estimated using the following assumptions:

	THREE MONTHS ENDED MARCH 31,	
	2020	2021
Expected term (in years)	6.0	—
Expected volatility	68.0%	—
Risk-free interest rate	1.5%	—
Expected dividend	—	—

AEROVATE THERAPEUTICS, INC.

NOTES TO UNAUDITED INTERIM CONDENSED FINANCIAL STATEMENTS

Stock-based compensation expense recognized for stock option grants has been reported in the statements of operations and comprehensive loss as follows (in thousands):

	THREE MONTHS ENDED MARCH 31,	
	2020	2021
Research and development	$ —	$ 12
General and administrative	7	11
Total	$ 7	$ 23

As of March 31, 2021, there was approximately $0.2 million of total unrecognized stock-based compensation expense related to nonvested stock-based compensation arrangements granted under the Plan, which is expected to be recognized over a weighted-average period of approximately 2.9 years.

(8) Related Party Transactions

Services Agreement

In August 2018, the Company entered into a services agreement ("Services Agreement") with Carnot, LLC ("Carnot"), an entity owned and controlled by RA Capital Management, L.P. under which Carnot provides research and other services to the Company. RA Capital Management, L.P. is a related party due to its equity ownership of the Company. The Company pays Carnot for services performed and costs incurred. The Services Agreement is for a term of two years. The Company may terminate the Services Agreement by giving 30 days' prior notice and either party can terminate the services agreement for a material breach, if not cured within 30 days following notice by the nonbreaching party.

In July 2019, the Services Agreement with Carnot was amended whereby research and other services are now performed by Carnot Pharma, LLC ("Carnot Pharma"), an entity owned and controlled by RA Capital Management, L.P., and the term was updated to the later of (i) two years from July 15, 2019 and (ii) completion of services under the agreement.

Expenses incurred by the Company under the Services Agreement with Carnot Pharma totaled $24,211 and $20,271 for the three months ended March 31, 2020 and 2021, respectively, and are presented in the statement of operations and comprehensive loss as research and development and general and administrative expenses. As of March 31, 2020 and 2021, $17,554 and $9,109, respectively, was due to Carnot Pharma, LLC by the Company for services rendered under the Services Agreement.

(9) Commitments and Contingencies

From time to time, the Company may become subject to claims or suits arising in the ordinary course of business. The Company accrues a liability for such matters when it is probable that future expenditures will be made and such expenditures can be reasonably estimated. As of December 31, 2020 and March 31, 2021, the Company is not a party to any litigation and has not recorded any such liabilities.

(10) Subsequent Events

The Company has evaluated subsequent events from the balance sheet date through June 9, 2021, the date the financial statements were available to be issued, except for the Reverse Stock Split described in Note 1, as to which the date is June 22, 2021.

In April 2021, the Company granted an aggregate of 1,701,543 ISOs and NSOs to certain of its employees and nonemployees under the Plan, each with an exercise price of $2.14 per share.

On June 4, 2021, upon the completion of the Second Milestone Closing and the Third Milestone Closing, the Company sold 29,338,346 shares of Series A redeemable convertible preferred stock at the Series A Original Issue Price for aggregate gross proceeds of $55.5 million.

8,682,142 Shares

Aerovate Therapeutics, Inc.

Common Stock

PROSPECTUS

Joint Book-Running Managers

Jefferies
Cowen
Evercore ISI

Lead Manager

Wedbush PacGrow

June 29, 2021