

VistaGen Therapeutics, Inc.
Form 424B5
August 31, 2017

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-215671
Prospectus Supplement
(To Prospectus Dated July 27, 2017)

1,371,430 Shares Common Stock

Series A1 Warrants to Purchase up to 1,388,931 Shares of Common Stock

Series A2 Warrants to Purchase up to 503,641 Shares of Common Stock

We are offering 1,371,430 shares of our common stock and warrants to purchase up to 1,892,572 shares of our common stock. Each share of our common stock is being sold together with 1.0128 Series A1 Warrants (Series A1 Warrants), each whole Series A1 Warrant to purchase one share of our common stock, and 0.3672 of a Series A2 Warrant (Series A2 Warrants), each whole Series A2 Warrant to purchase one share of our common stock. The Series A1 Warrants and the Series A2 Warrants are collectively referred to herein as the Warrants). Both Warrants will have an exercise price of \$1.82 per share. Each Series A1 Warrant will be exercisable for a five-year period commencing on March 7, 2018. Each Series A2 Warrant will be exercisable for a five-year period commencing on the date of issuance. The shares of our common stock and Warrants are immediately separable and will be issued separately, but will be purchased together in this offering. The shares of our common stock issuable from time to time upon exercise of the Warrants are also being offered pursuant to this prospectus supplement and the accompanying prospectus.

Our common stock is presently traded on the NASDAQ Capital Market under the symbol "VTGN." On August 30, 2017, the last reported sale price of our common stock was \$1.82 per share. There is no established trading market for the Warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the Warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the Warrants will be limited.

As of August 31, 2017, the aggregate market value of our voting and non-voting common stock held by non-affiliates pursuant to General Instruction I.B.6. of Form S-3 was \$18,843,006 which was calculated based on 9,191,710 outstanding shares of our voting and non-voting common stock held by non-affiliates and at a price of \$2.05 per share, the closing sale price of our common stock reported on The NASDAQ Capital Market on July 31, 2017. As a result, we are eligible to offer and sell up to an aggregate of \$6,280,374 of shares of our common stock pursuant to General Instruction I.B.6. of Form S-3. Following this offering, we will have sold securities with an aggregate market value of \$6,279,776 pursuant to General Instruction I.B.6. of Form S-3 during the prior 12 calendar month period that ends on, and includes, the date of this prospectus supplement.

Investing in the common stock involves risks. See "Risk Factors" beginning on page S-6 of this prospectus supplement.

Per Share and Related Warrants Total

Public offering price	\$1.75	\$2,400,003
Underwriting discount(1)	\$0.1225	\$168,000
Proceeds, before expenses, to us	\$1.6275	\$2,232,003

(1) We have agreed to reimburse the underwriters for certain expenses. See “Underwriting.”

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The underwriter expects to deliver the shares and related Warrants against payment on or about September 6, 2017.

Oppenheimer & Co.

The date of this prospectus supplement is August 31, 2017

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the SEC) utilizing a “shelf” registration process. This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of this offering. The second part, the accompanying prospectus, provides more general information about the securities we may offer from time to time, some of which may not apply to the securities offered by this prospectus supplement. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, and the additional information described under “Where You Can Find More Information” on page S-48 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference therein, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference therein.

Neither we nor the underwriters have authorized any other person to provide you with any information that is different. We are offering to sell, and seeking offers to buy, our securities only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the securities in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and/or the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus supplement and/or the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless the context otherwise requires, references in this prospectus supplement to “we”, “us” and “our” refer to VistaGen Therapeutics, Inc.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about our company, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus, in the documents we incorporate by reference and in any free writing prospectus that we have authorized for use in connection with this offering. This summary is not complete and does not contain all the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the “Risk Factors” contained in this prospectus supplement, the accompanying prospectus and the financial statements and the notes thereto incorporated by reference in this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Business Overview

We are a clinical-stage biopharmaceutical company focused on developing new generation medicines for depression and other central nervous system (CNS) disorders. Unless the context otherwise requires, the words “VistaGen Therapeutics, Inc.” “VistaGen,” “we,” “the Company,” “us” and “our” refer to VistaGen Therapeutics, Inc., a Nevada corporation. All references to future quarters and years in this prospectus supplement refer to calendar quarters and calendar years, unless reference is made otherwise.

AV-101 is our oral CNS product candidate in Phase 2 clinical development in the United States, initially as a new generation adjunctive treatment for Major Depressive Disorder (MDD) in patients with an inadequate response to standard antidepressants approved by the U.S. Food and Drug Administration (FDA). AV-101’s mechanism of action (MOA) involves both NMDA (N-methyl-D-aspartate) and AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors in the brain responsible for fast excitatory synaptic activity throughout the CNS. AV-101’s MOA is fundamentally differentiated from all FDA-approved antidepressants, as well as all atypical antipsychotics such as aripiprazole often used adjunctively to augment them. We believe AV-101 also has potential as a new treatment alternative for several additional CNS indications, including epilepsy, Huntington’s disease, levodopa (L-DOPA)-induced dyskinesia associated with Parkinson’s disease, and as a potential non-opioid treatment for neuropathic pain.

Clinical studies conducted at the U.S. National Institute of Mental Health (NIMH), part of the U.S. National Institutes of Health (NIH), by Dr. Carlos Zarate, Jr., Chief of the NIMH’s Experimental Therapeutics & Pathophysiology Branch and its Section on Neurobiology and Treatment of Mood and Anxiety Disorders, have focused on the antidepressant effects of low dose ketamine hydrochloride injection (ketamine), an ion-channel blocking NMDA receptor antagonist, in MDD patients with inadequate responses to multiple standard antidepressants. These NIMH studies, as well as clinical research at Yale University and other academic institutions, have demonstrated robust antidepressant effects in treatment-resistant MDD patients within twenty-four hours of a single sub-anesthetic dose of ketamine administered by intravenous (IV) injection.

We believe orally-administered AV-101 may have potential to deliver ketamine-like antidepressant effects without ketamine’s psychological and other negative side effects. As published in the October 2015 issue of the peer-reviewed, *Journal of Pharmacology and Experimental Therapeutics*, in an article titled, “The prodrug 4-chlorokynurenine causes ketamine-like antidepressant effects, but not side effects, by NMDA/glycineB-site inhibition, using well-established preclinical models of depression, AV-101 was shown to induce fast-acting, dose-dependent, persistent and statistically significant antidepressant-like responses following a single treatment. These responses were equivalent to those seen with a single sub-anesthetic control dose of ketamine. In addition, these

studies confirmed that the fast-acting antidepressant effects of AV-101 were mediated through both inhibiting the GlyB site of the NMDA receptor and activating the AMPA receptor pathway in the brain.

Pursuant to our Cooperative Research and Development Agreement (CRADA) with the NIMH, the NIMH is funding, and Dr. Zarate, as Principal Investigator, and his team are conducting, a small Phase 2 clinical study of AV-101 monotherapy in subjects with treatment-resistant MDD (the NIMH AV-101 MDD Phase 2 Monotherapy Study). Subject to the satisfaction of certain requirements described more fully below, we intend to launch in the first quarter of 2018 a 180-patient Phase 2 multi-center, multi-dose, double blind, placebo-controlled efficacy and safety study of AV-101 as a new generation adjunctive treatment of MDD in adult patients with an inadequate response to standard, FDA-approved antidepressants (the AV-101 MDD Phase 2 Adjunctive Treatment Study). Dr. Maurizio Fava, Professor of Psychiatry at Harvard Medical School and Director, Division of Clinical Research, Massachusetts General Hospital (MGH) Research Institute, will be the Principal Investigator of our AV-101 MDD Phase 2 Adjunctive Treatment Study. Dr. Fava was the co-Principal Investigator with Dr. A. John Rush of the STAR*D study, the largest clinical trial conducted in depression to date, whose findings were published in journals such as the New England Journal of Medicine (NEJM) and the Journal of the American Medical Association (JAMA). We expect to complete this study by the end of 2018, with top line results available in the first quarter of 2019.

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VistaStem Therapeutics (VistaStem) is our wholly owned subsidiary focused on applying human pluripotent stem cell (hPSC) technology, internally and with collaborators, to discover, rescue, develop and commercialize (i) proprietary new chemical entities (NCEs) for CNS and other diseases and (ii) regenerative medicine (RM) involving hPSC-derived blood, cartilage, heart and liver cells. Our internal drug rescue programs are designed to utilize CardioSafe 3D, our customized cardiac bioassay system, to develop small molecule NCEs for our pipeline. To advance potential RM applications of its cardiac stem cell technology, in December 2016, VistaStem exclusively sublicensed to BlueRock Therapeutics LP, a next generation RM company established by Bayer AG and Versant Ventures, rights to certain proprietary technologies relating to the production of cardiac stem cells for the treatment of heart disease (the BlueRock Agreement). In a manner similar to its exclusive sublicense agreement with BlueRock Therapeutics, VistaStem may pursue additional RM collaborations or licensing transactions involving blood, cartilage, and/or liver cells derived from hPSCs for (A) cell-based therapy, (B) cell repair therapy, and/or (C) tissue engineering.

Recent Developments

Spring 2017 Private Placement

Between late-March 2017 and August 2017, we sold to accredited investors, in a self-placed private placement, units consisting of an aggregate of 523,572 unregistered shares of our common stock and warrants to purchase up to an aggregate of 276,071 unregistered shares of our common stock pursuant to which we received proceeds of approximately \$1.04 million (the Spring 2017 Private Placement). Included with the accredited investors that participated in the Spring 2017 Private Placement was Dr. Jerry Gin, a member of our Board of Directors, and his spouse, who together purchased an aggregate total of 100,000 shares of unregistered common stock and warrants to purchase up to 50,000 shares of common stock for an aggregate purchase price of \$200,000.

AV-101 and Major Depressive Disorder

Background

The World Health Organization (WHO) estimates that 300 million people worldwide are affected by depression. According to the NIH, major depression is one of the most common mental disorders in the U.S. The NIMH reports that, in 2014, approximately 16 million adults in the U.S. had at least one major depressive episode in the past year. According to the U.S. Centers for Disease Control and Prevention (CDC) one in 10 Americans over the age of 12 takes a standard, FDA-approved antidepressant.

Most standard antidepressants target neurotransmitter reuptake inhibition – either serotonin (antidepressants known as SSRIs) or serotonin/norepinephrine (antidepressants known as SNRIs). Even when effective, these standard depression medications take many weeks to achieve adequate antidepressant effects. Nearly two out of every three drug-treated depression patients do not obtain adequate therapeutic benefit from initial treatment with a standard antidepressant. Even after treatment with many different standard antidepressants, nearly one out of every three drug-treated depression patients still do not achieve adequate therapeutic benefits from their antidepressant medication. Such patients with an inadequate response to standard antidepressants often seek to augment their treatment regimen by adding an atypical antipsychotic (drugs such as aripiprazole), despite only modest potential therapeutic benefit and the significant risk of additional side effects.

All standard antidepressants have risks of side effects, including, among others, anxiety, metabolic syndrome, sleep disturbance and sexual dysfunction. Adjunctive use of atypical antipsychotics to augment inadequately performing standard antidepressants may increase the risk of significant side effects, including, tardive dyskinesia, substantial

weight gain, diabetes and heart disease, while offering only a modest potential increase in therapeutic benefit.

AV-101

AV-101 is our oral CNS product candidate in Phase 2 development in the United States, initially focused as a new generation antidepressant for the adjunctive treatment of MDD patients with an inadequate response to standard, FDA-approved antidepressants. As published in the October 2015 issue of the peer-reviewed, Journal of Pharmacology and Experimental Therapeutics, in an article titled, The prodrug 4-chlorokynurenine causes ketamine-like antidepressant effects, but not side effects, by NMDA/glycineB-site inhibition, using well-established preclinical models of depression, AV-101 was shown to induce fast-acting, dose-dependent, persistent and statistically significant ketamine-like antidepressant effects following a single treatment, responses equivalent to those seen with a single sub-anesthetic control dose of ketamine, without the negative side effects seen with ketamine. In addition, these studies confirmed that the antidepressant effects of AV-101 were mediated through both inhibition of the GlyB site of NMDA receptors and activation of the AMPA receptor pathway in the brain, a key final common pathway feature of certain new generation antidepressants such as ketamine and AV-101, each with a MOA that is fundamentally different from all standard antidepressants and atypical antipsychotics used adjunctively to augment them.

We have completed two NIH-funded, randomized, double blind, placebo-controlled AV-101 Phase 1 safety studies. Currently, pursuant to our CRADA with the NIMH and Dr. Carlos Zarate, Jr., the NIMH is funding, and Dr. Zarate, as Principal Investigator, and his team are conducting, a small NIMH AV-101 MDD Phase 2 Monotherapy Study. Although we are not involved in conducting this study, we currently anticipate that the NIMH will complete the NIMH AV-101 MDD Phase 2 Monotherapy Study during the first half of 2018.

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We intend to launch a 180-patient AV-101 MDD Phase 2 Study in the first quarter of 2018, focused on using AV-101 as an adjunctive treatment of MDD in patients with an inadequate response to standard, FDA-approved antidepressants. In connection with our preparation to commence this study and to improve the efficiency of our existing method of manufacturing AV-101 drug substance for this and later studies, we, together with our contract manufacturing organization (CMO), developed a novel process for the chemical synthesis of the AV-101 drug substance which we believe will significantly reduce the current and future cost of manufacturing AV-101 drug substance and improve the yield of AV-101 drug substance manufactured. While developing this new manufacturing process, our CMO produced a batch of AV-101 drug substance that contained impurities in excess of regulatory guidelines which, although technically applicable only to New Drug Applications, are applied as common practice and industry standard to development stage programs. Consequently, the FDA placed a clinical hold on the launch of our AV-101 MDD Phase 2 Adjunctive Treatment Study until such time as we are able to demonstrate that impurities in the AV-101 drug substance manufactured with our new manufacturing process are within applicable regulatory guidelines. As a result of further refinement of our new manufacturing process, we have and are able to produce AV-101 drug substance that meets the applicable regulatory specifications. Accordingly, we believe our current AV-101 drug substance, produced using our new manufacturing method, meets all applicable regulatory guidelines.

The FDA also requested reproductive toxicology studies that are routinely conducted later in stages of clinical development. Available toxicology studies for AV-101 do not suggest any reproductive organ involvement, however we have implemented additional contraceptive measures in the revised study protocol that will remain in effect until reproductive toxicology studies are completed. Although not a basis for the current clinical hold, we plan to confirm with FDA that the recently implemented contraceptive measures address concerns for the current stage of development. We believe the data from our new manufacturing process, together with other requested revisions to our IND application, will satisfy the FDA's concerns and we expect to receive FDA approval in the fourth quarter of 2017 to proceed with the AV-101 MDD Phase 2 Adjunctive Treatment Study. However, no assurance can be given that the FDA will lift the clinical hold and permit us to proceed with the AV-101 MDD Phase 2 Adjunctive Treatment Study or as to the timing of any such action.

We believe preclinical studies and Phase 1 safety studies support our hypothesis that AV-101 may also have potential to treat multiple additional CNS disorders and diseases beyond MDD, including epilepsy, neuropathic pain, Huntington's disease, L-DOPA-induced dyskinesia associated with Parkinson's disease, and other CNS indications where modulation of the NMDA receptor, activation of AMPA pathways and/or key active metabolites of AV-101 may achieve therapeutic benefit. We are beginning to plan additional Phase 2 clinical studies of AV-101 to further evaluate its therapeutic potential beyond MDD.

CardioSafe 3D™; NCE Drug Rescue and Regenerative Medicine

VistaStem Therapeutics is our wholly owned subsidiary focused on applying hPSC technology to discover, rescue, develop and commercialize proprietary small molecule NCEs for CNS and other diseases, as well as potential cellular therapies involving stem cell-derived blood, cartilage, heart and liver cells. CardioSafe 3D™ is our customized in vitro cardiac bioassay system capable of predicting potential human heart toxicity of small molecule NCEs in vitro, long before they are ever tested in animal and human studies. Potential commercial applications of our stem cell technology platform involve using CardioSafe 3D internally for NCE drug discovery and drug rescue to expand our proprietary drug candidate pipeline. Drug rescue involves leveraging substantial prior research and development investments by pharmaceutical companies and others related to public domain NCE programs terminated before FDA approval due to heart toxicity risks and RM and cellular therapies. To advance potential RM applications of its cardiac stem cell technology, in December 2016, VistaStem exclusively sublicensed to BlueRock Therapeutics LP, a next generation regenerative medicine company established by Bayer AG and Versant Ventures, rights to certain proprietary technologies relating to the production of cardiac stem cells for the treatment of heart disease. In a manner

similar to the BlueRock Agreement, VistaStem may also pursue additional potential RM applications using blood, cartilage, and/or liver cells derived from hPSCs for (A) cell-based therapy (injection of stem cell-derived mature organ-specific cells obtained through directed differentiation), (B) cell repair therapy (induction of regeneration by biologically active molecules administered alone or produced by infused genetically engineered cells), or (C) tissue engineering (transplantation of in vitro grown complex tissues) using hPSC-derived blood, bone, cartilage, and/or liver cells.

Corporate Information

VistaGen Therapeutics, Inc., a Nevada corporation, is the parent of VistaGen Therapeutics, Inc. (dba VistaStem Therapeutics, Inc.), a wholly-owned California corporation founded in 1998. Our principal executive offices are located at 343 Allerton Avenue, South San Francisco, California 94080, and our telephone number is (650) 577-3600. Our website address is www.vistagen.com. The information contained on our website is not part of this prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website.

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THE OFFERING

Issuer VistaGen Therapeutics, Inc.

Common Stock Offered by Us 1,371,430 shares of common stock.

Common Stock to be Outstanding Immediately After this Offering 10,751,474 shares.

Warrants Offered by Us Warrants to purchase up to 1,892,572 shares of common stock, consisting of Series A1 Warrants to purchase up to 1,388,931 shares of common stock and Series A2 Warrants to purchase up to 503,641 shares of common stock. Each share of our common stock is being sold together with 1.0128 Series A1 Warrants, each whole Series A1 Warrant to purchase one share of our common stock, and 0.3672 of a Series A2 Warrant, each whole Series A2 Warrant to purchase one share of our common stock. Each of the Warrants will have an exercise price of \$1.82 per share. The Series A1 Warrants will be exercisable for a five-year period commencing on March 7, 2018. Each Series A2 Warrant will be exercisable for a five-year period commencing on the date of issuance.

This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of the Warrants. The exercise price of the Warrants and the number of shares into which the Warrants may be exercised are subject to adjustment in certain circumstances. See “Description of Securities we are Offering” on page S-44.

Use of Proceeds We currently intend to use the net proceeds from the sale of the securities offered by this prospectus supplement for general corporate purposes, including research and development related to preparations for our planned AV-101 MDD Phase 2 Adjunctive Treatment Study, and working capital. See “Use of Proceeds” on page S-42.

Risk Factors Investing in our common shares and Warrants involves a high degree of risk. For a discussion of factors that you should consider before buying our securities, see the information under “Risk Factors” in this prospectus supplement and under similar headings in the documents incorporated by reference into this prospectus supplement.

NASDAQ Capital Market symbol “VTGN.”

There is no established trading market for the Warrants and we do not expect a market to develop. In addition, we do not intend to apply for the listing of the Warrants on any national securities exchange or other trading market. Without an active trading market, the liquidity of the Warrants will be limited.

The number of shares of our common stock that will be outstanding immediately after the offering is based on 9,380,044 shares outstanding as of August 31, 2017. Unless we specifically state otherwise, the share information in

this prospectus supplement excludes:

2,509,871 shares of common stock reserved for issuance upon exercise of outstanding stock options under our 1999 Stock Incentive Plan and our Amended and Restated 2016 Stock Incentive Plan, with a weighted average exercise price of \$3.74 per share;

329,662 shares of common stock reserved for future issuance in connection with future grants under our Amended and Restated 2016 Stock Incentive Plan;

4,825,078 shares of common stock that have been reserved for issuance upon exercise of outstanding warrants, with a weighted average exercise price of \$6.17 per share;

750,000 shares of common stock reserved for issuance upon conversion of 500,000 shares our Series A Preferred;

1,160,240 shares of common stock reserved for issuance upon conversion of 1,160,240 shares of our Series B Preferred and 663,460 shares of common stock for issuance as payment of accrued dividends on outstanding shares of Series Preferred;

2,318,012 shares of common stock reserved for issuance upon conversion of 2,318,012 shares of our Series C Preferred; and

1,892,572 shares of common stock issuable upon the exercise of the Warrants offered hereby.

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RISK FACTORS

An investment in our securities involves a high degree of risk. You should consider the risks, uncertainties and assumptions discussed below, together with all of the other information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, including our Annual Report on Form 10-K for the fiscal year ended March 31, 2017, as well as subsequently filed Quarterly Reports on Form 10-Q with the SEC. It is not possible to predict or identify all such risks. Consequently, we could also be affected by additional factors that are not presently known to us or that we currently consider to be immaterial to our operations. The occurrence of any of these known or unknown risks might cause you to lose all or part of your investment in the offered securities.

Risks Related to Product Development, Regulatory Approval and Commercialization

We depend heavily on the success of AV-101. We cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize AV-101, or any product candidate.

We currently have no drug products for sale and may never be able to develop and commercialize marketable drug products. Our business depends heavily on the successful development, regulatory approval and commercialization of AV-101 for depression, including for MDD, and, potentially, various other diseases and disorders involving the CNS, as well as, but to a more limited extent, our ability to produce, develop and commercialize NCEs from our drug rescue programs. AV-101 will require substantial additional non-clinical and clinical development, testing and regulatory approval before it may be commercialized. It is unlikely to achieve regulatory approval, if at all, until at least 2021. Each drug rescue NCE will require substantial non-clinical development, all phases of clinical development, and regulatory approval before it may be commercialized. The non-clinical and clinical development of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must demonstrate through non-clinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of any of our non-clinical or clinical studies. This process can take many years and may also include post-marketing studies and surveillance, which will require the expenditure of substantial resources beyond the proceeds we have raised to date. Of the large number of drugs in development in the United States, only a small percentage will successfully complete the FDA regulatory approval process and will be commercialized. Accordingly, even if we are able to obtain the requisite financing to continue to fund our non-clinical and clinical studies, we cannot assure you that AV-101, any drug rescue NCE, or any other future product candidate will be successfully developed or commercialized.

We are not permitted to market our product candidates in the United States until we receive approval of a New Drug Application (NDA) from the FDA, or in any foreign countries until we receive the requisite approval from such countries. We expect the FDA to require us to complete the planned AV-101 MDD Phase 2 Adjunctive Treatment Study and at least two pivotal Phase 3 clinical trials in order to submit an NDA for AV-101 as an adjunctive treatment for MDD patients with an inadequate response to standard, FDA-approved antidepressants. Also, we anticipate that the FDA will require that we conduct additional toxicity studies, additional non-clinical and certain small clinical studies before submitting an NDA for AV-101. The results of all of these studies are not known until after the studies are concluded.

Obtaining FDA approval of an NDA is a complex, lengthy, expensive and uncertain process, and the FDA may delay, limit or deny approval of AV-101 or any of our product candidates for many reasons, including, among others:

if we submit an NDA and it is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional non-clinical or clinical studies, limitations on approved labeling or distribution and use restrictions;

the FDA may require development of a Risk Evaluation and Mitigation Strategy (REMS) as a condition of approval or post-approval;

the FDA or the applicable foreign regulatory agency may determine that the manufacturing processes or facilities of third-party contract manufacturers with which we contract do not conform to applicable requirements, including current Good Manufacturing Practices (cGMPs); or

the FDA or applicable foreign regulatory agency may change its approval policies or adopt new regulations.

Any of these factors, many of which are beyond our control, could jeopardize our ability to obtain regulatory approval for and successfully commercialize AV-101 or any other product candidate we may develop, including drug rescue NCEs. Any such setback in our pursuit of regulatory approval for any product candidate would have a material adverse effect on our business and prospects.

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We intend to seek a Fast Track designation from the FDA for AV-101, initially for adjunctive treatment of MDD patients with an inadequate response to standard antidepressants. Even if the FDA approves Fast Track designation for AV-101 for this indication, it may not actually lead to a faster development or regulatory review or approval process.

The Fast Track designation is a program offered by the FDA pursuant to certain mandates under the FDA Modernization Act of 1997, designed to facilitate drug development and to expedite the review of new drugs that are intended to treat serious or life threatening conditions. Compounds selected must demonstrate the potential to address unmet medical needs. The Fast Track designation allows for close and frequent interaction with the FDA. A designated Fast Track drug may also be considered for priority review with a shortened review time, rolling submission, and accelerated approval if applicable. The designation does not, however, guarantee approval or expedited approval of any application for the product.

We intend to seek FDA Fast Track designation for AV-101, initially for adjunctive treatment of MDD patients with an inadequate response to standard antidepressants, and we may do so for other CNS indications, as well as for other product candidates. The FDA has broad discretion whether or not to grant a Fast Track designation, and even if we believe AV-101 and other product candidates are eligible for this designation, we cannot be sure that the review or approval will compare to conventional FDA procedures. Even if granted, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development programs.

The number of patients suffering from MDD has not been established with precision. If the actual number of patients with MDD is smaller than we anticipate, we or our collaborators may encounter difficulties in enrolling patients in AV-101 clinical trials, including the NIMH AV-101 MDD Phase 2 Monotherapy Study and our planned AV-101 MDD Phase 2 Adjunctive Treatment Study, thereby delaying completion such studies or preventing additional clinical development. Further, if AV-101 is approved for adjunctive treatment of MDD patients with an inadequate response to standard antidepressants, and the market for this indication is smaller than we anticipate, our ability to achieve profitability could be limited.

Results of earlier clinical trials may not be predictive of the results of later-stage clinical trials.

The results of preclinical studies and early clinical trials of AV-101 and other product candidates, including positive results, may not be predictive of the results of later-stage clinical trials. AV-101 or other product candidates in later stages of clinical trials may fail to show the desired safety and efficacy results despite having progressed through preclinical studies and initial clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier studies. Similarly, our future clinical trial results may not be successful for these or other reasons.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials nonetheless failed to obtain FDA approval. We have not yet completed a Phase 2 clinical trial for AV-101, and if the NIMH fails to produce positive results in the NIMH AV-101 MDD Phase 2 Monotherapy Study, the development timeline and regulatory approval and commercialization prospects for AV-101 and, correspondingly, our business and financial prospects, could be materially adversely affected.

This drug candidate development risk is heightened by any changes in planned timing or nature of clinical trials compared to completed clinical trials. As product candidates are developed through preclinical to early and late stage clinical trials towards approval and commercialization, it is customary that various aspects of the development program, such as manufacturing and methods of administration, are altered along the way in an effort to optimize

processes and results. While these types of changes are common and are intended to optimize the product candidates for later stage clinical trials, approval and commercialization, such changes do carry the risk that they will not achieve these intended objectives.

For example, the results of planned clinical trials may be adversely affected if we or our collaborator seek to optimize and scale-up production of a product candidate. In such case, we will need to demonstrate comparability between the newly manufactured drug substance and/or drug product relative to the previously manufactured drug substance and/or drug product. Demonstrating comparability may cause us to incur additional costs or delay initiation or completion of our clinical trials, including the need to initiate a dose escalation study and, if unsuccessful, could require us to complete additional non-clinical or clinical studies of our product candidates.

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If serious adverse events or other undesirable side effects are identified during the use of AV-101 in clinical trials, it may adversely affect our development of AV-101 for MDD and other CNS indications.

AV-101 as a monotherapy is currently being tested by the NIMH in an NIMH-investigator sponsored Phase 2 clinical trial for the treatment of MDD and may be subjected to testing in the future for other CNS indications in additional investigator sponsored clinical trials. If serious adverse events or other undesirable side effects, or unexpected characteristics of AV-101 are observed in investigator sponsored clinical trials of AV-101 or our clinical trials, it may adversely affect or delay our clinical development of AV-101, and the occurrence of these events would have a material adverse effect on our business.

Failures or delays in the commencement or completion of our planned clinical trials and non-clinical studies of our product candidates could result in increased costs to us and could delay, prevent or limit our ability to generate revenue and continue our business.

Under our CRADA, the NIMH is conducting and funding the NIMH AV-101 MDD Phase2 Monotherapy Study. We will need to complete the planned AV-101 MDD Phase 2 Adjunctive Treatment Study, at least two additional large Phase 2b/3 clinical trials, additional toxicity and non-clinical studies and certain smaller clinical studies prior to the submission of an NDA for AV-101 as a new generation adjunctive treatment for MDD. Successful completion of our clinical trials is a prerequisite to submitting an NDA to the FDA and, consequently, the ultimate approval and commercial marketing of AV-101 for MDD and any other product candidates we may develop. Except as disclosed herein, we do not know whether the NIMH AV-101 MDD Phase 2 Monotherapy Study, the AV-101 MDD Phase 2 Adjunctive Treatment Study or any of our future-planned non-clinical and clinical trials will be completed on schedule, if at all, as the commencement and completion of non-clinical and clinical trials can be delayed or prevented for a number of reasons, including, among others:

the FDA may deny permission to proceed with our planned clinical trials or any other clinical trials we may initiate, or may place a planned or ongoing clinical trial on hold, including the clinical hold on the launch of our planned AV-101 MDD Phase 2 Adjunctive Treatment Study;

delays in filing or receiving approvals of additional INDs that may be required;

negative results from our ongoing non-clinical studies;

delays in reaching or failing to reach agreement on acceptable terms with prospective 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;

inadequate quantity or quality of a product candidate or other materials necessary to conduct non-clinical or clinical trials, including delays in the manufacturing of sufficient supply or finished drug product resulting from our new manufacturing process for AV-101;

difficulties obtaining Institutional Review Board (IRB) approval to conduct a clinical trial at a prospective site or sites;

challenges in recruiting and enrolling patients to participate in clinical trials, including the proximity of patients to clinical trial sites;

eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications;

severe or unexpected drug-related side effects experienced by patients in a clinical trial;

delays in validating any endpoints utilized in a clinical trial;

the FDA may disagree with our clinical trial design and our interpretation of data from prior non-clinical studies or clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our clinical trials;

reports from non-clinical or clinical testing of other CNS indications or therapies that raise safety or efficacy concerns; and

difficulties retaining patients who have enrolled in a clinical trial but may be prone to withdraw due to rigors of the clinical trials, lack of efficacy, side effects, personal issues or loss of interest.

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Clinical trials may also be delayed or terminated prior to completion as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRBs at the sites where the IRBs are overseeing a clinical trial, a data and safety monitoring board (DSMB), overseeing the clinical trial at issue or other regulatory authorities due to a number of factors, including, among others:

failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;

inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities that reveals deficiencies or violations that require us to undertake corrective action, including the imposition of a clinical hold;

unforeseen safety issues, including any that could be identified in our ongoing non-clinical carcinogenicity studies, adverse side effects or lack of effectiveness;

changes in government regulations or administrative actions;

problems with clinical supply materials that may lead to regulatory actions, such as the clinical hold currently imposed by the FDA; and

lack of adequate funding to continue clinical trials.

Changes in regulatory requirements, FDA guidance or unanticipated events during our non-clinical studies and clinical trials of our product candidates may occur, which may result in changes to non-clinical studies and clinical trial protocols or additional non-clinical studies and clinical trial requirements, which could result in increased costs to us and could delay our development timeline.

Changes in regulatory requirements, FDA guidance or unanticipated events during our non-clinical studies and clinical trials may force us to amend non-clinical studies and clinical trial protocols or the FDA may impose additional non-clinical studies and clinical trial requirements. Amendments or changes to our clinical trial protocols would require resubmission to the FDA and IRBs for review and approval, which may adversely impact the cost, timing or successful completion of clinical trials. Similarly, amendments to our non-clinical studies may adversely impact the cost, timing, or successful completion of those non-clinical studies. If we experience delays completing, or if we terminate, any of our non-clinical studies or clinical trials, or if we are required to conduct additional non-clinical studies or clinical trials, the commercial prospects for our product candidates may be harmed and our ability to generate product revenue will be delayed.

We rely, and expect that we will continue to rely, on third parties to conduct non-clinical and clinical trials of AV-101 and any other product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, completion of non-clinical and clinical trials and development of AV-101 and other product candidates may be delayed and we may not be able to obtain regulatory approval for or commercialize AV-101 or other product candidates and our business could be substantially harmed.

We do not have the internal staff resources to independently conduct non-clinical and clinical trials completely on our own. We rely on our strategic relationships with various medical institutions, non-clinical and clinical investigators, contract laboratories and other third parties, such as contract research and development organizations (CROs), to conduct non-clinical and clinical trials of our product candidates. We enter into agreements with third-party CROs to provide monitors for and to manage data for our clinical trials, as well as provide other services necessary to prepare for, conduct and complete clinical trials. We rely heavily on these and other third-parties for execution of non-clinical and clinical trials for our product candidates and control only certain aspects of their activities. As a result, we have less direct control over the conduct, timing and completion of these non-clinical and clinical trials and the management of data developed through non-clinical and clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with outside parties can also be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Outside parties may:

have staffing difficulties and/or undertake obligations beyond their anticipated capabilities and resources;

fail to comply with contractual obligations;

experience regulatory compliance issues;

undergo changes in priorities or become financially distressed; or

form relationships with other entities, some of which may be our competitors.

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These factors may materially adversely affect the willingness or ability of third parties to conduct our non-clinical and clinical trials and may subject us to unexpected cost increases that are beyond our control. Nevertheless, we are responsible for ensuring that each of our non-clinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific requirements and standards, and our reliance on CROs or the NIH does not relieve us of our regulatory responsibilities. We and our CROs and the NIMH are required to comply with regulations and guidelines, including current cGCPs for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the trial patients are adequately informed of the potential risks of participating in clinical trials. These regulations are enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for any products in clinical development. The FDA enforces cGCP regulations through periodic inspections of clinical trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that, upon inspection, the FDA will determine that any of our clinical trials comply with cGCPs. In addition, our clinical trials must be conducted with product candidates produced under cGMPs regulations and will require a large number of test patients. Our failure or the failure of our CROs to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process and could also subject us to enforcement action up to and including civil and criminal penalties.

Although we design our clinical trials for our product candidates, we plan to have CROs, and in the case of the NIMH AV-101 MDD Phase 2 Monotherapy Study, the NIMH, conduct the AV-101 Phase 2 and Phase 3 clinical trials. As a result, many important aspects of our drug development programs are outside of our direct control. In addition, the CROs or the NIMH, as the case may be, may not perform all of their obligations under arrangements with us or in compliance with regulatory requirements, but we remain responsible and are subject to enforcement action that may include civil penalties up to and including criminal prosecution for any violations of FDA laws and regulations during the conduct of our clinical trials. If the NIMH or CROs do not perform clinical trials in a satisfactory manner, breach their obligations to us or fail to comply with regulatory requirements, the development and commercialization of AV-101 and other product candidates may be delayed or our development program materially and irreversibly harmed. We cannot control the amount and timing of resources these CROs or the NIMH devote to our program or our clinical products. If we are unable to rely on non-clinical and clinical data collected by our CROs or the NIMH, we could be required to repeat, extend the duration of, or increase the size of our clinical trials and this could significantly delay commercialization and require significantly greater expenditures.

If any of our relationships with these third-party CROs or the NIMH terminate, we may not be able to enter into arrangements with alternative CROs or collaborators. If CROs or the NIMH do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, any clinical trials that such CROs or the NIMH are associated with may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for or successfully develop and commercialize our product candidates. As a result, we believe that our financial results and the commercial prospects for our product candidates in the subject indication would be harmed, our costs would increase and our ability to generate revenue would be delayed.

We rely completely on third-parties to manufacture and prepare our clinical supplies of AV-101 and other product candidates, and we intend to rely on third parties to produce non-clinical, clinical and commercial supplies of AV-101 and any future product candidate.

We do not currently have, nor do we plan to acquire, the infrastructure or capability to internally manufacture our drug supply of AV-101 or any other product candidates for use in the conduct of our non-clinical studies and clinical trials, and we lack the internal resources and the capability to manufacture any product candidates on a research, development or commercial scale. The facilities used by our contract manufacturers to manufacture the active pharmaceutical ingredient and final drug product must complete a pre-approval inspection by the FDA and other comparable foreign regulatory agencies to assess compliance with applicable requirements, including cGMPs, after we submit our NDA or relevant foreign regulatory submission to the applicable regulatory agency.

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We do not directly control the manufacturing process of, and are completely dependent on, our contract manufacturers to comply with cGMPs for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or applicable foreign regulatory agencies, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities, or the FDA may take other actions, including the imposition of the clinical hold disclosed above. In addition, we have no direct control over our contract manufacturers' ability to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such other companies, which exposes our third-party contract manufacturers to regulatory risks for the production of such materials and products. As a result, failure to satisfy the regulatory requirements for the production of those materials and products may affect the regulatory clearance of our contract manufacturers' facilities generally or affect the timing of our clinical trials, including the imposition of clinical hold disclosed above. If the FDA or an applicable foreign regulatory agency determines now or in the future that these facilities for the manufacture of our product candidates are noncompliant, we may need to find alternative manufacturing facilities, which would adversely impact our ability to develop, obtain regulatory approval for or market our product candidates. Our reliance on contract manufacturers also exposes us to the possibility that they, or third parties with access to their facilities, will have access to and may appropriate our trade secrets or other proprietary information.

We do not yet have long-term supply agreements in place with our contract manufacturers and each batch of our product candidates are individually contracted under a quality and supply agreement. If we engage new contract manufacturers, such contractors must complete an inspection by the FDA and other applicable foreign regulatory agencies. We plan to continue to rely upon contract manufacturers and, potentially, collaboration partners, to manufacture research, development and commercial quantities of AV-101 and other product candidates, if approved. Our current scale of manufacturing for AV-101 is adequate to support our currently planned needs for additional non-clinical studies and clinical trials.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval for and commercialize AV-101 and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system, including the ACA, that could, among other things, prevent or delay marketing approval of AV-101, restrict or regulate post-approval activities, and affect our ability to profitably sell any products for which we obtain marketing approval.

In March 2010, the ACA was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry, and impose additional health policy reforms. The law has continued the downward pressure on pharmaceutical pricing, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. We cannot predict the full impact of the ACA on pharmaceutical companies, as many of the reforms require the promulgation of detailed regulations implementing the statutory provisions, some of which have not yet fully occurred.

Further, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. In January 2017, the President of the United States signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In May 2017, the United States House of Representatives passed legislation known as the American

Health Care Act, which, if enacted, would amend or repeal significant portions of the ACA. The United States Senate could adopt the American Health Care Act as passed by the United States House of Representatives or other legislation to amend or replace elements of the ACA. Thus, it is uncertain when or if the American Health Care Act will become law. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, the President of the United States signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This included further reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional Congressional action is taken. Additionally, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period in which the government may recover overpayments to providers from three to five years. Further, 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, review the relationship between pricing and manufacturer patient programs, reduce the out-of-pocket cost of prescription drugs, and reform government program reimbursement methodologies for drugs.

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Moreover, the Drug Supply Chain Security Act, which was enacted in 2012 as part of the Food and Drug Administration Safety and Innovation Act, imposes new obligations on manufacturers of pharmaceutical products related to product tracking and tracing. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We are not sure whether additional legislative changes will be enacted, or whether the current regulations, guidance or interpretations will be changed, or what the impact of such changes on our business, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

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

Even if we receive marketing approval for our product candidates in the United States, we may never receive regulatory approval to market our product candidates outside of the United States.

We have not yet selected any markets outside of the United States where we intend to seek regulatory approval to market our product candidates. In order to market any product outside of the United States, however, we must establish and comply with the numerous and varying safety, efficacy and other regulatory requirements of other countries. Approval procedures vary among countries and can involve additional product candidate testing and additional administrative review periods. The time required to obtain approvals in other countries might differ from that required to obtain FDA approval. The marketing approval processes in other countries may implicate all of the risks detailed above regarding FDA approval in the United States as well as other risks. In particular, in many countries outside of the United States, products must receive pricing and reimbursement approval before the product can be commercialized. Obtaining this approval can result in substantial delays in bringing products to market in such countries. Marketing approval in one country does not ensure marketing approval in another, but a failure or delay in obtaining marketing approval in one country may have a negative effect on the regulatory process in others. Failure to obtain marketing approval in other countries or any delay or other setback in obtaining such approval would impair our ability to market our product candidates in such foreign markets. Any such impairment would reduce the size of our potential market, which could have a material adverse impact on our business, results of operations and prospects.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to generate any revenue.

We do not currently have an infrastructure for the sale, marketing and distribution of pharmaceutical products, nor do we intend to create such capabilities. Therefore, in order to market our product candidates, if approved by the FDA or any other regulatory body, we must make contractual arrangements with third parties to perform services related to sales, marketing, managerial and other non-technical capabilities relating to the commercialization of our product candidates. If we are unable to establish adequate contractual arrangements for such sales, marketing and distribution capabilities, or if we are unable to do so on commercially reasonable terms, our business, results of operations, financial condition and prospects will be materially adversely affected.

Even if we receive marketing approval for our product candidates, our product candidates may not achieve broad market acceptance, which would limit the revenue that we generate from their sales.

The commercial success of our product candidates, if approved by the FDA or other applicable regulatory authorities, will depend upon the awareness and acceptance of our product candidates among the medical community, including physicians, patients and healthcare payors. Market acceptance of our product candidates, if approved, will depend on a

number of factors, including, among others:

the efficacy and safety of our product candidates as demonstrated in clinical trials, and, if required by any applicable regulatory authority in connection with the approval for the applicable indications, to provide patients with incremental health benefits, as compared with other available therapies;

limitations or warnings contained in the labeling approved for our product candidates by the FDA or other applicable regulatory authorities;

the clinical indications for which our product candidates are approved;

availability of alternative treatments already approved or expected to be commercially launched in the near future;

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the potential and perceived advantages of our product candidates over current treatment options or alternative treatments, including future alternative treatments;

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

the strength of marketing and distribution support and timing of market introduction of competitive products;

publicity concerning our products or competing products and treatments;

pricing and cost effectiveness;

the effectiveness of our sales and marketing strategies;

our ability to increase awareness of our product candidates through marketing efforts;

our ability to obtain sufficient third-party coverage or reimbursement; or

the willingness of patients to pay out-of-pocket in the absence of third-party coverage.

If our product candidates are approved but do not achieve an adequate level of acceptance by patients, physicians and payors, we may not generate sufficient revenue from our product candidates to become or remain profitable. Before granting reimbursement approval, healthcare payors may require us to demonstrate that our product candidates, in addition to treating these target indications, also provide incremental health benefits to patients. Our efforts to educate the medical community and third-party payors about the benefits of our product candidates may require significant resources and may never be successful.

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

Undesirable safety concerns and side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt non-clinical studies and clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities.

Further, clinical trials by their nature utilize a sample of potential patient populations. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable safety concerns or side effects caused by such

product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

regulatory authorities may withdraw or limit their approval of such product candidates;

regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;

we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;

we may be subject to regulatory investigations and government enforcement actions;

we may decide to remove such product candidates from the marketplace;

we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and

our reputation may suffer.

We believe that any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and would substantially increase the costs of commercializing our product candidates and significantly impact our ability to successfully commercialize our product candidates and generate revenues.

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Even if we receive marketing approval for our product candidates, we may still face future development and regulatory difficulties.

Even if we receive marketing approval for our product candidates, regulatory authorities may still impose significant restrictions on our product candidates, indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. Our product candidates will also be subject to ongoing regulatory requirements governing the labeling, packaging, storage and promotion of the product and record keeping and submission of safety and other post-market information. The FDA has significant post-marketing authority, including, for example, the authority to require labeling changes based on new safety information and to require post-marketing studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA or post-approval, the submission of a REMS. Any REMS required by the FDA may lead to increased costs to assure compliance with new post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue.

Manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMPs and other regulations. If we or a regulatory agency discover problems with our product candidates, such as adverse events of unanticipated severity or frequency, or problems with the facility where our product candidates are manufactured, a regulatory agency may impose restrictions on our product candidates, the manufacturer or us, including requiring withdrawal of our product candidates from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may, among other things:

issue warning letters or untitled letters;

seek an injunction or impose civil or criminal penalties or monetary fines;

suspend or withdraw marketing approval;

suspend any ongoing clinical trials;

refuse to approve pending applications or supplements to applications submitted by us;

suspend or impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products, refuse to permit the import or export of products, or require that we initiate a product recall.

Competing therapies could emerge adversely affecting our opportunity to generate revenue from the sale of our product candidates.

The pharmaceuticals industry is highly competitive. There are many public and private pharmaceutical companies, universities, governmental agencies and other research organizations actively engaged in the research and development of product candidates that may be similar to our product candidates or address similar markets. It is probable that the number of companies seeking to develop product candidates similar to our product candidates will increase.

Currently, management is unaware of any FDA-approved oral adjunctive therapy for MDD patients with an inadequate response to standard antidepressants having the same mechanism of action and safety profile as AV-101. However, new antidepressant products with other mechanisms of action or products approved for other indications, including the anesthetic ketamine hydrochloride, are being or may be used off-label for treatment of MDD, as well as other CNS indications for which AV-101 may have therapeutic potential. Additionally, other non-pharmaceutical treatment options, such as psychotherapy and electroconvulsive therapy (ECT) are sometimes used before or instead of standard antidepressant medications to treat patients with MDD.

In the field of new generation, orally available, adjunctive treatments of adult MDD patients with an inadequate response to standard antidepressants, we believe our principal competitor is Alkermes' orally available drug candidate in Phase 3 development, ALKS-5461.

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Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and the commercialization of those treatments. We believe that a range of pharmaceutical and biotechnology companies have programs to develop small molecule drug candidates for the treatment of depression, including MDD, epilepsy, neuropathic pain, dyskinesia associated with L-DOPA therapy for Parkinson's disease and other neurological conditions and diseases, including, but not limited to, Abbott Laboratories, Acadia, Allergan, Alkermes, Astra Zeneca, Eli Lilly, GlaxoSmithKline, IntraCellular, Johnson & Johnson/Janssen, Lundbeck, Merck, Novartis, Ono, Otsuka, Pfizer, Roche, Sage, Sumitomo Dainippon, and Takeda, as well as any affiliates of the foregoing companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

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

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for 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 evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential markets for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate 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 collaboration could be more attractive than the one with us for our product candidate. The terms of any collaboration or other arrangements that we may establish may not be favorable to us.

We may also be restricted under existing 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 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 the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, 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 our product candidates or bring them to market and generate product revenue.

In addition, any future collaboration 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.

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We may not be successful in our efforts to identify or discover additional product candidates or we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates with commercial and therapeutic potential. Although AV-101 is in Phase 2 clinical development for treatment of depression, we may fail to pursue additional CNS-related Phase 2 development opportunities for AV-101, or identify additional product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying new product candidates or our product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

Because we currently have limited financial and management resources, we necessarily focus on a limited number of research and development programs and product candidates and are currently focused primarily on development of AV-101, with additional limited focus on NCE drug rescue and RM. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other potential CNS-related indications for AV-101 that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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

We are subject to healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Although we do not currently have any products on the market, once we begin commercializing our products, we may be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of our product candidates, if approved. Our future arrangements with third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our product candidates, if we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

The federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid.

The federal False Claims Act imposes criminal and civil penalties, including those from civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government.

The federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

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The federal transparency requirements, sometimes referred to as the “Sunshine Act,” under the Patient Protection and Affordable Care Act, require manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests.

Analogous state laws and regulations, such as state anti-kickback and false claims laws and transparency laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance.

Guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and drug pricing.

Ensuring that our future business arrangements with third parties comply with applicable healthcare laws and regulations could be costly. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations, including anticipated activities to be conducted by our sales team, were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines and exclusion from government funded healthcare programs, such as Medicare and Medicaid, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The FDA and other regulatory agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. If we are found to have improperly promoted off-label uses, 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, such as AV-101, if approved. In particular, a product may not be promoted for uses that are not approved by the FDA or such other regulatory agencies as reflected in the product’s approved labeling. For example, if we receive marketing approval for AV-101 as an adjunctive treatment of MDD, physicians may nevertheless prescribe AV-101 to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. 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.

Even if approved, reimbursement policies could limit our ability to sell our product candidates.

Market acceptance and sales of our product candidates will depend heavily on reimbursement policies and may be affected by healthcare reform measures. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels for those medications. Cost containment is a primary concern in the U.S. healthcare industry and elsewhere. Government authorities and these third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that reimbursement will be available for our product candidates and, if reimbursement is available, the level of such reimbursement. Reimbursement may impact the demand for, or the price of, our product candidates. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates.

In some foreign countries, particularly in Canada and European countries, the pricing of prescription pharmaceuticals is subject to strict governmental control. In these countries, pricing negotiations with governmental authorities can take six months or longer after the receipt of regulatory approval and product launch. To obtain favorable reimbursement for the indications sought or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates with other available therapies. If reimbursement for our product candidates is unavailable in any country in which we seek reimbursement, if it is limited in scope or amount, if it is conditioned upon our completion of additional clinical trials, or if pricing is set at unsatisfactory levels, our operating results could be materially adversely affected.

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We may seek FDA Orphan Drug designation for one or more of our product candidates, including AV-101. Even if we have obtained FDA Orphan Drug designation for AV-101 of other product candidates, there may be limits to the regulatory exclusivity afforded by such designation.

We may, in the future, choose to seek FDA Orphan Drug designation for one or more of our product candidates, including AV-101. Even if we obtain Orphan Drug designation from the FDA for AV-101 or any other product candidates, there are limitations to the exclusivity afforded by such designation. In the United States, the company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years. This orphan drug exclusivity prevents the FDA from approving another application, including a full NDA to market the same drug for the same orphan indication, except in very limited circumstances, including when the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. For purposes of small molecule drugs, the FDA defines “same drug” as a drug that contains the same active moiety and is intended for the same use as the drug in question. To obtain Orphan Drug status for a drug that shares the same active moiety as an already approved drug, it must be demonstrated to the FDA that the drug is safer or more effective than the approved orphan designated drug, or that it 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. 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 quantity of the drug to meet the needs of patients with the rare disease or condition or if another drug with the same active moiety is determined to be safer, more effective, or represents a major contribution to patient care.

Our future growth may depend, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future profitability may depend, in part, on our ability to commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. If we commercialize our product candidates in foreign markets, we would be subject to additional risks and uncertainties, including:

our customers’ ability to obtain reimbursement for our product candidates in foreign markets;

our inability to directly control commercial activities because we are relying on third parties;

the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements;

different medical practices and customs in foreign countries affecting acceptance in the marketplace;

import or export licensing requirements;

longer accounts receivable collection times;

longer lead times for shipping;

language barriers for technical training;

reduced protection of intellectual property rights in some foreign countries;

the existence of additional potentially relevant third party intellectual property rights;

foreign currency exchange rate fluctuations; and

the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

Foreign sales of our product candidates could also be adversely affected by the imposition of governmental controls, political and economic instability, trade restrictions and changes in tariffs.

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We are a development stage biopharmaceutical company with no current revenues or approved products, and limited experience developing new drug, biological and/or regenerative medicine candidates, including conducting clinical trials and other areas required for the successful development and commercialization of therapeutic products, which makes it difficult to assess our future viability.

We are a development stage biopharmaceutical company. Although our lead drug candidate is in Phase 2 development, we currently have no approved products and currently generate no revenues, and we have not yet fully demonstrated an ability to overcome many of the fundamental risks and uncertainties frequently encountered by development stage companies in new and rapidly evolving fields of technology, particularly biotechnology. To execute our business plan successfully, we will need to accomplish the following fundamental objectives, either on our own or with strategic collaborators:

produce product candidates;

develop and obtain required regulatory approvals for commercialization of product candidates we produce;

maintain, leverage and expand our intellectual property portfolio;

establish and maintain sales, distribution and marketing capabilities, and/or enter into strategic partnering arrangements to access such capabilities;

gain market acceptance for our products; and

obtain adequate capital resources and manage our spending as costs and expenses increase due to research, production, development, regulatory approval and commercialization of product candidates.

Our future success is highly dependent upon our ability to successfully develop and commercialize AV-101 and discover, as well as produce, develop and commercialize proprietary drug rescue NCEs using our stem cell technology, and we cannot provide any assurance that we will successfully develop and commercialize AV-101 or drug rescue NCEs, or that, if produced, AV-101 or any drug rescue NCE will be successfully commercialized.

Research programs designed to identify and produce drug rescue NCEs require substantial technical, financial and human resources, whether or not any NCEs are ultimately identified and produced. In particular, our drug rescue programs may initially show promise in identifying potential NCEs, yet fail to yield a lead NCE suitable for preclinical, clinical development or commercialization for many reasons, including the following:

our drug rescue research and development methodology may not be successful in identifying and developing potential drug rescue NCEs;

competitors may develop alternatives that render our drug rescue NCEs obsolete;

a drug rescue NCE may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;

a drug rescue NCE may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or

a drug rescue NCE may not be accepted as safe and effective by regulatory authorities, patients, the medical community or third-party payors.

In addition, we do not have a sales or marketing infrastructure, and we, including our executive officers, do not have any significant pharmaceutical sales, marketing or distribution experience. We may seek to collaborate with others to develop and commercialize AV-101, drug rescue NCEs and/or other product candidates if and when they are developed. If we enter into arrangements with third parties to perform sales, marketing and distribution services for our products, the resulting revenues or the profitability from these revenues to us are likely to be lower than if we had sold, marketed and distributed our products ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute AV-101, any drug rescue NCEs or other product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, in collaboration with third parties, we will not be successful in commercializing our product candidates.

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We have limited operating history with respect to drug development, including our anticipated focus on the identification and assessment of potential drug rescue NCEs and no operating history with respect to the production of drug rescue NCEs, and we may never be able to produce a drug rescue NCE.

If we are unable to develop and commercialize AV-101 or produce suitable drug rescue NCEs, we may not be able to generate sufficient revenues to execute our business plan, which likely would result in significant harm to our financial position and results of operations, which could adversely impact our stock price.

There are a number of factors, in addition to the utility of CardioSafe 3D, that may impact our ability to identify and produce, develop or out-license and commercialize drug rescue NCEs, independently or with strategic partners, including:

our ability to identify potential drug rescue candidates in the public domain, obtain sufficient quantities of them, and assess them using our bioassay systems;

if we seek to rescue drug rescue candidates that are not available to us in the public domain, the extent to which third parties may be willing to out-license or sell certain drug rescue candidates to us on commercially reasonable terms;

our medicinal chemistry collaborator's ability to design and produce proprietary drug rescue NCEs based on the novel biology and structure-function insight we provide using CardioSafe 3D; and

financial resources available to us to develop and commercialize lead drug rescue NCEs internally, or, if we out-license them to strategic partners, the resources such partners choose to dedicate to development and commercialization of any drug rescue NCEs they license from us.

Even if we do produce proprietary drug rescue NCEs, we can give no assurance that we will be able to develop and commercialize them as a marketable drug, on our own or in collaboration with others. Before we generate any revenues from AV-101 and/or additional drug rescue NCEs we or our potential collaborators must complete preclinical and clinical developments, submit clinical and manufacturing data to the FDA, qualify a third party contract manufacturer, receive regulatory approval in one or more jurisdictions, satisfy the FDA that our contract manufacturer is capable of manufacturing the product in compliance with cGMP, build a commercial organization, make substantial investments and undertake significant marketing efforts ourselves or in partnership with others. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates.

If CardioSafe 3D fails to predict accurately and efficiently the cardiac effects, both toxic and nontoxic, of drug rescue candidates and drug rescue NCEs, then our drug rescue programs will be adversely affected.

Our success is partly dependent on our ability to use CardioSafe 3D to identify and predict, accurately and efficiently, the potential toxic and nontoxic cardiac effects of drug rescue candidates and drug rescue NCEs. If CardioSafe 3D is not capable of providing physiologically relevant and clinically predictive information regarding human cardiac biology, our drug rescue business will be adversely affected.

CardioSafe 3D may not be meaningfully more predictive of the behavior of human cells than existing methods.

The success of our drug rescue programs is highly dependent upon CardioSafe 3D being more accurate, efficient and clinically predictive than long-established surrogate safety models, including animal cells and live animals, and immortalized, primary and transformed cells, currently used by pharmaceutical companies and others. We cannot give assurance that CardioSafe 3D will be more efficient or accurate at predicting the heart safety of new drug candidates than the testing models currently used. If CardioSafe 3D fails to provide a meaningful difference compared to existing or new models in predicting the behavior of human heart, respectively, their utility for drug rescue will be limited and our drug rescue business will be adversely affected.

We may invest in producing drug rescue NCEs for which there proves to be no demand.

To generate revenue from our drug rescue activities, we must produce proprietary drug rescue NCEs for which there proves to be demand within the healthcare marketplace, and, if we intend to out-license a particular drug rescue NCE for development and commercialization prior to market approval, then also among pharmaceutical companies and other potential collaborators. However, we may produce drug rescue NCEs for which there proves to be no or limited demand in the healthcare market and/or among pharmaceutical companies and others. If we misinterpret market conditions, underestimate development costs and/or seek to rescue the wrong drug rescue candidates, we may fail to generate sufficient revenue or other value, on our own or in collaboration with others, to justify our investments, and our drug rescue business may be adversely affected.

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We may experience difficulty in producing human cells and our future stem cell technology research and development efforts may not be successful within the timeline anticipated, if at all.

Our human pluripotent stem cell technology is technically complex, and the time and resources necessary to develop various human cell types and customized bioassay systems are difficult to predict in advance. We might decide to devote significant personnel and financial resources to research and development activities designed to expand, in the case of drug rescue, and explore, in the case of drug discovery and regenerative medicine, potential applications of our stem cell technology platform. In particular, we may conduct exploratory non-clinical RM programs involving blood, bone, cartilage, and/or liver cells. Although we and our collaborators have developed proprietary protocols for the production of multiple differentiated cell types, we could encounter difficulties in differentiating and producing sufficient quantities of particular cell types, even when following these proprietary protocols. These difficulties could result in delays in production of certain cells, assessment of certain drug rescue candidates and drug rescue NCEs, design and development of certain human cellular assays and performance of certain exploratory non-clinical regenerative medicine studies. In the past, our stem cell research and development projects have been significantly delayed when we encountered unanticipated difficulties in differentiating human pluripotent stem cells into heart and liver cells. Although we have overcome such difficulties in the past, we may have similar delays in the future, and we may not be able to overcome them or obtain any benefits from our future stem cell technology research and development activities. Any delay or failure by us, for example, to produce functional, mature blood, bone, cartilage, and liver cells could have a substantial and material adverse effect on our potential drug discovery, drug rescue and regenerative medicine business opportunities and results of operations.

Restrictions on research and development involving human embryonic stem cells and religious and political pressure regarding such stem cell research and development could impair our ability to conduct or sponsor certain potential collaborative research and development programs and adversely affect our prospects, the market price of our common stock and our business model.

Some of our research and development programs may involve the use of human cells derived from our controlled differentiation of human embryonic stem cells (hESCs). Some believe the use of hESCs gives rise to ethical and social issues regarding the appropriate use of these cells. Our research related to differentiation of hESCs may become the subject of adverse commentary or publicity, which could significantly harm the market price of our common stock. Although now substantially less than in years past, certain political and religious groups in the United States and elsewhere voice opposition to hESC technology and practices. We may use hESCs derived from excess fertilized eggs that have been created for clinical use in in vitro fertilization (IVF) procedures and have been donated for research purposes with the informed consent of the donors after a successful IVF procedure because they are no longer desired or suitable for IVF. Certain academic research institutions have adopted policies regarding the ethical use of human embryonic tissue. These policies may have the effect of limiting the scope of future collaborative research opportunities with such institutions, thereby potentially impairing our ability to conduct certain research and development in this field that we believe is necessary to expand the drug rescue capabilities of our technology, which would have a material adverse effect on our business.

The use of embryonic or fetal tissue in research (including the derivation of hESCs) in other countries is regulated by the government, and varies widely from country to country. Government-imposed restrictions with respect to use of hESCs in research and development could have a material adverse effect on us by harming our ability to establish critical collaborations, delaying or preventing progress in our research and development, and causing a decrease in the market interest in our stock.

The foregoing potential ethical concerns do not apply to our use of induced pluripotent stem cells (iPSCs) because their derivation does not involve the use of embryonic tissues.

We have assumed that the biological capabilities of iPSCs and hESCs are likely to be comparable. If it is discovered that this assumption is incorrect, our exploratory research and development activities focused on potential regenerative medicine applications of our stem cell technology platform could be harmed.

We may use both hESCs and iPSCs to produce human cells for our customized in vitro assays for drug discovery and drug rescue purposes. However, we anticipate that our future exploratory research and development, if any, focused on potential regenerative medicine applications of our stem cell technology platform primarily will involve iPSCs. With respect to iPSCs, we believe scientists are still somewhat uncertain about the clinical utility, life span, and safety of such cells, and whether such cells differ in any clinically significant ways from hESCs. If we discover that iPSCs will not be useful for whatever reason for potential regenerative medicine programs, this would negatively affect our ability to explore expansion of our platform in that manner, including, in particular, where it would be preferable to use iPSCs to reproduce rather than approximate the effects of certain specific genetic variations.

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If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions, which could have a material adverse effect on our operations.

To the extent our research and development activities involve using iPSCs, we will be subject to complex and evolving laws and regulations regarding privacy and informed consent. Many of these laws and regulations are subject to change and uncertain interpretation, and could result in claims, changes to our research and development programs and objectives, increased cost of operations or otherwise harm the Company.

To the extent that we pursue research and development activities involving iPSCs, we will be subject to a variety of laws and regulations in the United States and abroad that involve matters central to such research and development activities, including obligations to seek informed consent from donors for the use of their blood and other tissue to produce, or have produced for us, iPSCs, as well as state and federal laws that protect the privacy of such donors. United States federal and state and foreign laws and regulations are constantly evolving and can be subject to significant change. If we engage in iPSC-related research and development activities in countries other than the United States, we may become subject to foreign laws and regulations relating to human subjects research and other laws and regulations that are often more restrictive than those in the United States. In addition, both the application and interpretation of these laws and regulations are often uncertain, particularly in the rapidly evolving stem cell technology sector in which we operate. These laws and regulations can be costly to comply with and can delay or impede our research and development activities, result in negative publicity, increase our operating costs, require significant management time and attention and subject us to claims or other remedies, including fines or demands that we modify or cease existing business practices.

Legal, social and ethical concerns surrounding the use of iPSCs, biological materials and genetic information could impair our operations.

To the extent that our future stem cell research and development activities involve the use of iPSCs and the manipulation of human tissue and genetic information, the information we derive from such iPSC-related research and development activities could be used in a variety of applications, which may have underlying legal, social and ethical concerns, including the genetic engineering or modification of human cells, testing for genetic predisposition for

certain medical conditions and stem cell banking. Governmental authorities could, for safety, social or other purposes, call for limits on or impose regulations on the use of iPSCs and genetic testing or the manufacture or use of certain biological materials involved in our iPSC-related research and development programs. Such concerns or governmental restrictions could limit our future research and development activities, which could have a material adverse effect on our business, financial condition and results of operations.

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Our human cellular bioassay systems and human cells we derive from human pluripotent stem cells, although not currently subject to regulation by the FDA or other regulatory agencies as biological products or drugs, could become subject to regulation in the future.

The human cells we produce from hPSCs and our customized bioassay systems using such cells, including CardioSafe 3D, are not currently sold, for research purposes or any other purpose, to biotechnology or pharmaceutical companies, government research institutions, academic and nonprofit research institutions, medical research organizations or stem cell banks, and they are not therapeutic procedures. As a result, they are not subject to regulation as biological products or drugs by the FDA or comparable agencies in other countries. However, if, in the future, we seek to include human cells we derive from hPSCs in therapeutic applications or product candidates, such applications and/or product candidates would be subject to the FDA's pre- and post-market regulations. For example, if we seek to develop and market human cells we produce for use in performing regenerative medicine applications, such as tissue engineering or organ replacement, we would first need to obtain FDA pre-market clearance or approval. Obtaining such clearance or approval from the FDA is expensive, time-consuming and uncertain, generally requiring many years to obtain, and requiring detailed and comprehensive scientific and clinical data. Notwithstanding the time and expense, these efforts may not result in FDA approval or clearance. Even if we were to obtain regulatory approval or clearance, it may not be for the uses that we believe are important or commercially attractive.

Risks Related to Our Financial Position

We have incurred significant net losses since inception and we will continue to incur substantial operating losses for the foreseeable future. We may never achieve or sustain profitability, which would depress the market price of our common stock, and could cause you to lose all or a part of your investment.

We have incurred significant net losses in each fiscal year since our inception in 1998, including net losses of \$10.3 million and \$47.2 million, which includes \$26.7 million of non-cash expense related to the extinguishment of essentially all of our outstanding promissory notes and certain other indebtedness, during the fiscal years ended March 31, 2017 and 2016, respectively. We incurred a net loss of approximately \$2.3 million in the quarter ended June 30, 2017 and, as of that date, we had an accumulated deficit of approximately \$144.3 million. We do not know whether or when we will become profitable. Substantially all of our operating losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity (deficit) and working capital. We expect our research and development expenses to significantly increase in connection with non-clinical studies and clinical trials of our product candidates. In addition, if we obtain marketing approval for our product candidates, we may incur significant sales, marketing and outsourced-manufacturing expenses should we elect not to collaborate with one or more third parties for such services and capabilities. As a public company, we incur additional costs associated with operating as a public company. As a result, we expect to continue to incur significant and increasing operating losses for the foreseeable future. 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 ability to become profitable depends upon our ability to generate revenues. To date, we have generated approximately \$17.7 million in revenues, including receipt of non-dilutive cash payments from collaborators, sublicense revenue, and research and development grant awards from the NIH, not including the fair market value of the ongoing NIMH AV-101 MDD Phase 2 Monotherapy Study under our NIMH CRADA. We have not yet commercialized any product or generated any revenues from product sales, and we do not know when, or if, we will

generate any revenue from product sales. We do not expect to generate significant revenue unless and until we obtain marketing approval of, and begin to experience sales of, AV-101, or we enter into one or more development and commercialization agreements with respect to AV-101 or one or more other product candidates. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

initiate and successfully complete non-clinical and clinical trials that meet their prescribed endpoints;

initiate and successfully complete all safety studies required to obtain U.S. and foreign marketing approval for our product candidates;

commercialize our product candidates, if approved, by developing a sales force or entering into collaborations with third parties; and

achieve market acceptance of our product candidates in the medical community and with third-party payors.

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Unless we enter into a development and commercialization collaboration or partnership agreement, we expect to incur significant sales and marketing costs as we prepare to commercialize AV-101 or other product candidates. Even if we initiate and successfully complete pivotal clinical trials of AV-101 or other product candidates, and AV-101 or other product candidates are approved for commercial sale, and despite expending these costs, AV-101 or other product candidates may not be commercially successful. We may not achieve profitability soon after generating product sales, if ever. If we are unable to generate product revenue, we will not become profitable and may be unable to continue operations without continued funding.

We require additional financing to execute our business plan and continue to operate as a going concern.

Our audited consolidated financial statements for the year ended March 31, 2017 as well as the unaudited condensed consolidated financial statements for the period ended June 30, 2017 included elsewhere in this Report have been prepared assuming we will continue to operate as a going concern, although we and our auditors have indicated that our continuing losses and negative cash flows from operations raise substantial doubt about our ability to continue as such. Because we continue to experience net operating losses, our ability to continue as a going concern is subject to our ability to obtain necessary funding from outside sources, including obtaining additional funding from the sale of our securities or obtaining loans and grant awards from financial institutions and/or government agencies where possible. Our continued net operating losses increase the difficulty in completing such sales or securing alternative sources of funding, and there can be no assurances that we will be able to obtain such funding on favorable terms or at all. If we are unable to obtain sufficient financing from the sale of our securities or from alternative sources, we may be required to reduce, defer, or discontinue certain or all of our research and development activities or we may not be able to continue as a going concern.

Since our inception, most of our resources have been dedicated to research and development of AV-101 and the drug rescue capabilities of our stem cell technology platform. In particular, we have expended substantial resources advancing AV-101 through preclinical development and Phase 1 clinical safety studies, and developing CardioSafe 3D and our cardiac stem cell technology for drug rescue and potential regenerative medicine applications, and we will continue to expend substantial resources for the foreseeable future developing and commercializing AV-101 for multiple CNS indications, and, potentially, developing drug rescue NCEs and RM therapies, on our own or in collaborations similar to the BlueRock Agreement. These expenditures will include costs associated with general and administrative costs, facilities costs, research and development, acquiring new technologies, manufacturing product candidates, conducting preclinical experiments and clinical trials and obtaining regulatory approvals, as well as commercializing any products approved for sale.

At June 30, 2017, our existing cash and cash equivalents were not sufficient to fund our current operations for the next 12 months or to complete our proposed AV-101 MDD Phase 2 Adjunctive Treatment Study. Further, we have no current source of revenue to sustain our present activities, and we do not expect to generate revenue until, and unless, we (i) out-license or sell AV-101, a drug rescue NCE, and/or another drug candidate unrelated to AV-101 to third-parties, (ii) enter into license arrangements involving our stem cell technology, or (iii) obtain approval from the FDA or other regulatory authorities and successfully commercialize, on our own or through a future collaboration, one or more of our compounds.

As the outcome of our AV-101 and NCE drug rescue activities and future anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates, on our own or in collaboration with others. In addition, other unanticipated costs may arise. As a result of these and other factors, we will need to seek additional capital in the near term to meet our future operating requirements, including capital necessary to develop, obtain regulatory approval for, and to commercialize our product candidates, and may seek additional capital in the event there exists favorable

market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. We are considering a range of potential sources of funding, including public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches, and we may complete additional financing arrangements in 2017 and beyond. Raising funds in the current economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Our future capital requirements depend on many factors, including:

the number and characteristics of the product candidates we pursue, including AV-101 and drug rescue NCEs;

the scope, progress, results and costs of researching and developing our product candidates, and conducting preclinical and clinical studies;

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the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates;

the cost of commercialization activities if any of our product candidates are approved for sale, including marketing, sales and distribution costs;

the cost of manufacturing our product candidates and any products we successfully commercialize;

our ability to establish and maintain strategic partnerships, licensing or other arrangements and the financial terms of such agreements;

market acceptance of our products;

the effect of competing technological and market developments;

our ability to obtain government funding for our programs;

the costs involved in obtaining and enforcing patents to preserve our intellectual property;

the costs involved in defending against such claims that we infringe third-party patents or violate other intellectual property rights and the outcome of such litigation;

the timing, receipt and amount of potential future licensee fees, milestone payments, and sales of, or royalties on, our future products, if any; and

the extent to which we acquire or invest in businesses, products and technologies, although we currently have no commitments or agreements relating to any of these types of transactions.

Any additional fundraising efforts will divert certain members of our management team from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts, in a timely manner, or on terms acceptable to us, if at all, and the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity securities and the conversion or exchange of certain of our outstanding securities will dilute all of our stockholders. The incurrence of debt could result in increased fixed payment obligations and we could be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or

license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidate or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain additional funding on a timely basis and on acceptable terms, we may be required to significantly curtail, delay or discontinue one or more of our research or product development programs or the commercialization of any product candidate or be unable to continue or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

We have identified material weaknesses in our internal control over financial reporting, and our business and stock price may be adversely affected if we do not adequately address those weaknesses or if we have other material weaknesses or significant deficiencies in our internal control over financial reporting.

We have identified material weaknesses in our internal control over financial reporting. In particular, we concluded that (i) the size and capabilities of the Company's staff does not permit appropriate segregation of duties to prevent one individual from overriding the internal control system by initiating, authorizing and completing all transactions, and (ii) the Company utilizes accounting software that does not prevent erroneous or unauthorized changes to previous reporting periods and/or can be adjusted so as to not provide an adequate auditing trail of entries made in the accounting software (See Item 9A. Controls and Procedures contained in our Annual Report on Form 10-K for the year ended June 30, 2017, filed with the SEC on June 29, 2017.).

The existence of one or more material weaknesses or significant deficiencies could result in errors in our financial statements, and substantial costs and resources may be required to rectify any internal control deficiencies. If we cannot produce reliable financial reports, investors could lose confidence in our reported financial information, we may be unable to obtain additional financing to operate and expand our business and our business and financial condition could be harmed.

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Raising additional capital will cause dilution to our existing stockholders, may restrict our operations or require us to relinquish rights, and may require us to seek stockholder approval to authorize additional shares of our common stock.

We intend to pursue private and public equity offerings, debt financings, strategic collaborations and licensing arrangements during 2017 and beyond. To the extent that we raise additional capital through the sale of common stock or securities convertible or exchangeable into common stock, or to the extent, for strategic purposes, we convert or exchange certain of our outstanding securities into common stock, our current stockholders' ownership interest in our company will be diluted. In addition, the terms of any such securities may include liquidation or other preferences that materially adversely affect rights of our stockholders. Debt financing, if available, would increase our fixed payment obligations and 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 additional funds through collaboration, strategic partnerships and licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our intellectual property, future revenue streams or grant licenses on terms that are not favorable to us.

We currently have 30.0 million shares of common stock authorized for issuance. Based on the current number of shares of our common stock: (i) outstanding, (ii) reserved for conversion or exchange of our various series of outstanding preferred stock, including for payment of accrued dividends on our outstanding Series B Preferred, (iii) reserved for the exercise of outstanding warrants, and (iv) reserved for the exercise of options granted or available for grant pursuant to our equity incentive plans, at June 30, 2017, we have approximately 8.1 million shares of common stock available for future financing or other activities. We anticipate seeking stockholder approval to amend our Articles of Incorporation to increase the number of shares of common stock we are authorized to issue in order to achieve our near-term or longer-term financing objectives.

Some of our programs have been partially supported by government grant awards, which may not be available to us in the future.

Since inception, we have received substantial funds under grant award programs funded by state and federal governmental agencies, such as the NIH, the NIH's National Institute of Neurological Disease and Stroke (NINDS) and the NIMH, and the California Institute for Regenerative Medicine (CIRM). To fund a portion of our future research and development programs, we may apply for additional grant funding from such or similar governmental organizations. However, funding by these governmental organizations may be significantly reduced or eliminated in the future for a number of reasons. For example, some programs are subject to a yearly appropriations process in Congress. In addition, we may not receive funds under future grants because of budgeting constraints of the agency administering the program. Therefore, we cannot assure you that we will receive any future grant funding from any government organization or otherwise. A restriction on the government funding available to us could reduce the resources that we would be able to devote to future research and development efforts. Such a reduction could delay the introduction of new products and hurt our competitive position.

Our ability to use net operating losses to offset future taxable income is subject to certain limitations.

As of March 31, 2017, we had federal and state net operating loss carryforwards of \$77.1 million and \$67.6 million, respectively, which begin to expire in fiscal 2018. Under Section 382 of the Internal Revenue Code of 1986, as amended (the Code) changes in our ownership may limit the amount of our net operating loss carryforwards that could be utilized annually to offset our future taxable income, if any. This limitation would generally apply in the event of a cumulative change in ownership of our company of more than 50% within a three-year period. Any such limitation may significantly reduce our ability to utilize our net operating loss carryforwards and tax credit carryforwards before they expire. Any such limitation, whether as the result of future offerings, prior private placements, sales of our

common stock by our existing stockholders or additional sales of our common stock by us in the future, could have a material adverse effect on our results of operations in future years. We have not completed a study to assess whether an ownership change for purposes of Section 382 has occurred, or whether there have been multiple ownership changes since our inception, due to the significant costs and complexities associated with such study.

General Company-Related Risks

If we fail to attract and retain senior management and key scientific personnel, we may be unable to successfully produce, develop and commercialize AV-101, drug rescue NCEs, other potential product candidates and other commercial applications of our stem cell technology.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and scientific and technical personnel. We are highly dependent upon our Chief Executive Officer, President and Chief Scientific Officer, Chief Medical Officer and Chief Financial Officer, as well as other employees, consultants and scientific collaborators. As of the date of this Report, we have nine full-time employees, which may make us more reliant on our individual employees than companies with a greater number of employees. The loss of services of any of these individuals could delay or prevent the successful development of AV-101, drug rescue NCEs, other product candidates, and other applications of our stem cell technology, including our production and assessment of potential drug rescue NCEs or disrupt our administrative functions.

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Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense. We will need to hire additional personnel as we expand our research and development and administrative activities. We may not be able to attract and retain quality personnel on acceptable terms.

In addition, we rely on a diverse range of strategic consultants and advisors, including manufacturing, scientific and clinical development, and regulatory advisors, to assist us in designing and implementing our research and development and regulatory strategies and plans, including our AV-101 development and drug rescue strategies and plans. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

As we seek to advance development of AV-101 for MDD and other CNS-related conditions, as well as stem cell technology-related drug rescue and RM programs, we will need to expand our research and development capabilities and/or contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners and other third parties. Future growth will impose significant added responsibilities on members of management. Our future financial performance and our ability to develop and commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our research and development efforts effectively and hire, train and integrate additional management, administrative and technical personnel. The hiring, training and integration of new employees may be more difficult, costly and/or time-consuming for us because we have fewer resources than a larger organization. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing the company.

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

If we develop AV-101, drug rescue NCEs, other product candidates, or regenerative medicine product candidates, either on our own or in collaboration with others, we will face inherent risks of product liability as a result of the required clinical testing of such product candidates, and will face an even greater risk if we or our collaborators commercialize any such product candidates. For example, we may be sued if AV-101, any drug rescue NCE, other product candidate, or regenerative medicine product candidate we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. 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 products that we may develop;

injury to our reputation;

withdrawal of clinical trial participants;

costs to defend the related litigation;

a diversion of management's time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. Although we maintain liability insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, 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 capital to pay such amounts.

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As a public company, we incur significant administrative workload and expenses to comply with U.S. regulations and requirements imposed by The NASDAQ Stock Market concerning corporate governance and public disclosure.

As a public company with common stock listed on The NASDAQ Capital Market, we must comply with various laws, regulations and requirements, including certain provisions of the Sarbanes-Oxley Act of 2002, as well as rules implemented by the SEC and The NASDAQ Stock Market. Complying with these statutes, regulations and requirements, including our public company reporting requirements, continues to occupy a significant amount of the time of management and involves significant accounting, legal and other expenses. Furthermore, these laws, regulations and requirements require us to observe greater corporate governance practices than we have employed in the past, including, but not limited to maintaining a sufficient number of independent directors, increased frequency of board meetings, and holding annual stockholder meetings. Our efforts to comply with these regulations are likely to result in increased general and administrative expenses and management time and attention directed to compliance activities.

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 global political conditions, as well as general conditions in the global economy and in the global financial and stock markets. Global financial and political crises cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including, weakened demand for our product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our services. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party CMOs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

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

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for AV-101 or other product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or

damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed.

We may acquire businesses or products, or form strategic alliances, in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional businesses or products, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire businesses with promising markets or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to successfully integrate them with our existing operations and company culture. We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

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Risks Related to Our Intellectual Property Rights

If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions we consider are important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, to defend and enforce our patents, should they issue, to preserve the confidentiality of our trade secrets and to operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain the proprietary position of our product candidates. We own patent applications related to AV-101 and we own and have licensed patents and patent applications related to human pluripotent stem cell technology.

Although we have an issued patent relating to AV-101 in the European Union, we cannot yet provide any assurances that any of our numerous pending U.S. and additional foreign patent applications relating to AV-101 will mature into issued patents and, if they do, that such patents will include claims with a scope sufficient to protect AV-101 or otherwise provide any competitive advantage. Moreover, other parties may have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third-party patent positions may limit or even eliminate our ability to obtain patent protection.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any additional patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. U.S. patents and patent applications may also be subject to interference proceedings, ex parte reexamination, or inter partes review proceedings, supplemental examination and challenges in district court. Patents may be subjected to opposition, post-grant review, or comparable proceedings lodged in various foreign, both national and regional, patent offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates.

Furthermore, though a patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the

same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

Our ability to enforce our patent rights depends on our ability to detect infringement. It is difficult to detect infringers who do not advertise the components that are used in their products. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time-consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

In addition, proceedings to enforce or defend our patents could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any patents covering our product candidates are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered our product candidates, our financial position and results of operations would also be materially and adversely impacted.

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The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

any of our AV-101 or other pending patent applications, if issued, will include claims having a scope sufficient to protect AV-101 or any other products or product candidates, particularly considering that the compound patent to AV-101 has expired;

any of our pending patent applications will issue as patents at all;

we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire;

we were the first to make the inventions covered by each of our patents and pending patent applications;

we were the first to file patent applications for these inventions;

others will not develop similar or alternative technologies that do not infringe our patents;

others will not use pre-existing technology to effectively compete against us;

any of our patents, if issued, will be found to ultimately be valid and enforceable;

any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;

we will develop additional proprietary technologies or product candidates that are separately patentable; or

that our commercial activities or products will not infringe upon the patents or proprietary rights of others.

We also rely upon unpatented trade secrets, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could otherwise become known or be independently discovered by our competitors.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates, if approved.

Our success will depend in part on our ability to operate without infringing the intellectual property and proprietary rights of third parties. We cannot assure you that our business, products and methods do not or will not infringe the patents or other intellectual property rights of third parties.

The pharmaceutical industry is characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringes patent claims or other intellectual property rights held by them or that we are employing their proprietary technology without authorization. As we continue to develop and, if approved, commercialize our current product candidates and future product candidates, competitors may claim that our technology infringes their intellectual property rights as part of business strategies designed to impede our successful commercialization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, third parties may have currently pending patent applications that may later result in issued patents that our product candidates may infringe, or which such third parties claim are infringed by our technologies. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on us. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

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Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. Any claim relating to intellectual property infringement that is successfully asserted against us may require us to pay substantial damages, including treble damages and attorney's fees if we are found to be willfully infringing another party's patents, for past use of the asserted intellectual property and royalties and other consideration going forward if we are forced to take a license. In addition, if any such claim was successfully asserted against us and we could not obtain such a license, we may be forced to stop or delay developing, manufacturing, selling or otherwise commercializing our product candidates.

Even if we are successful in these proceedings, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following:

cease developing, selling or otherwise commercializing our product candidates;

pay substantial damages for past use of the asserted intellectual property;

obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and

in the case of trademark claims, redesign, or rename, some or all of our product candidates to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time-consuming.

Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects.

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

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could

result in substantial costs and be a distraction to management and other employees.

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 U.S. Patent and Trademark Office (USPTO), European Patent Office (EPO) and various other foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

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

Even if the patent applications we own or license are issued, competitors may infringe these patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States or European Union.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO or EPO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

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 product candidates in all countries and jurisdictions throughout the world is prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we 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. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For the patent applications relating to AV-101, as well as for many of the patent families that we own or license, the relevant statutory deadlines have not yet expired. Thus, for each of the patent families that we believe provide coverage for our lead product candidates or technologies, we will need to decide whether and where to pursue protection outside the United States.

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Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents 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 the infringement of our patents, if obtained, or the misappropriation of 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 the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought 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.

Furthermore, proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, 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 or license.

We are dependent, in part, on licensed intellectual property. If we were to lose our rights to licensed intellectual property, we may not be able to continue developing or commercializing our product candidates, if approved. If we breach any of the agreements under which we license the use, development and commercialization rights to our product candidates or technology from third parties or, in certain cases, we fail to meet certain development or payment deadlines, we could lose license rights that are important to our business.

We are a party to a number of license agreements under which we are granted rights to intellectual property that are or could become important to our business, and we expect that we may need to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose on us, various development, regulatory and/or commercial diligence obligations, payment of fees, milestones and/or royalties and other obligations. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to develop or market products, which could be covered by the license. Our business could suffer, for example, if any current or future licenses terminate, if the licensors fail to abide by the terms of the license, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. See “Business —Intellectual Property” herein for a description of our license agreements, which includes a description of the termination provisions of these agreements.

As we have done previously, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we cannot provide any assurances that third-party patents do not

exist that might be enforced against our current product candidates or future products in the absence of such a license. We may fail to obtain any of these licenses on commercially reasonable terms, if at all. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property subject to a license agreement, including:

the scope of rights granted under the license agreement and other interpretation-related issues;

whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

our right to sublicense patent and other rights to third parties under collaborative development relationships;

our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and

the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

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

We have entered into several licenses to support our various stem cell technology-related programs. We may enter into additional license(s) to third-party intellectual property that are necessary or useful to our business. Our current licenses and any future licenses that we may enter into impose various royalty payments, milestone, and other obligations on us. For example, the licensor may retain control over patent prosecution and maintenance under a license agreement, in which case, we may not be able to adequately influence patent prosecution or prevent inadvertent lapses of coverage due to failure to pay maintenance fees. If we fail to comply with any of our obligations under a current or future license agreement, our licensor(s) may allege that we have breached our license agreement and may accordingly seek to terminate our license with them. In addition, future licensor(s) may decide to terminate our license at will. Termination of any of our current or future licenses could result in our loss of the right to use the licensed intellectual property, which could materially adversely affect our ability to develop and commercialize a product candidate or product, if approved, as well as harm our competitive business position and our business prospects.

In addition, if our licensors fail to abide by the terms of the license, if the licensors fail to prevent infringement by third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms our business could suffer.

Some intellectual property which we have licensed may have been discovered through government funded programs and thus may be subject to federal regulations such as “march-in” rights, certain reporting requirements, and a preference for U.S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-U.S. manufacturers.

Some of the intellectual property rights we have licensed or license in the future may have been generated through the use of U.S. government funding and may therefore be subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980 (Bayh-Dole Act). These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). The U.S. government also has the right to take title to these inventions if we fail, or the applicable licensor fails, to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the U.S. government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us, or the applicable licensor, to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the U.S. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products

covered by such intellectual property.

In the event we apply for additional U.S. government funding, and we discover compounds or drug candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent terms and obtaining data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of the U.S. patents we own or license 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 permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. For example, we may not be granted an extension if the active ingredient of AV-101 is used in another drug company's product candidate and that product candidate is the first to obtain FDA approval. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our ability to generate revenues could be materially adversely affected.

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

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation: the Leahy-Smith America Invents Act, referred to as the America Invents Act. The America Invents Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. The full impact of these decisions is not yet known. For example, on March 20, 2012 in *Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al. v. Prometheus Laboratories, Inc.*, the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patentable subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013 in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA molecules are patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. Additionally, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the Myriad and Prometheus decisions. This guidance did not limit the application of Myriad to DNA but, rather, applied the decision to other natural products. Further, in 2015, in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, the Court of Appeals for the Federal Circuit held that methods for detecting fetal genetic defects were not patent eligible subject matter.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue in the future.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

Certain of our current employees have been, and certain of our future employees may have been, previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities.

Although we are not aware of any claims currently pending or threatened against us, we may be subject to claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We have and may

in the future also be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in defending such claims, in addition to paying monetary claims, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize our product candidates, which would materially adversely affect our commercial development efforts.

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Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

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, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The following examples are illustrative:

others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of patents, should such patents issue from our patent applications;

we might not have been the first to make the inventions covered by a pending patent application that we own;

we might not have been the first to file patent applications covering an invention;

others may independently develop similar or alternative technologies without infringing our intellectual property rights;

pending patent applications that we own or license may not lead to issued patents;

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

third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;

we may not be able to obtain and/or maintain necessary or useful licenses on reasonable terms or at all; 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 and results of operations.

If, instead of identifying drug rescue candidates based on information available to us in the public domain, we seek to in-license drug rescue candidates from biotechnology, medicinal chemistry and pharmaceutical companies, academic, governmental and nonprofit research institutions, including the NIH, or other third-parties, there can be no assurances that we will obtain material ownership or economic participation rights over intellectual property we may derive from such licenses or similar rights to the drug rescue NCEs we may produce and develop. If we are unable to obtain ownership or substantial economic participation rights over intellectual property related to drug rescue NCEs we produce and develop, our business may be adversely affected.

Risks Related to our Securities

The limited public market for our securities may adversely affect an investor's ability to liquidate an investment in the Company.

Our common stock is currently quoted on The NASDAQ Capital Market, however, there is presently limited trading activity. We can give no assurance that an active market will develop, or if developed, that it will be sustained. If an investor acquires shares of our common stock, the investor may not be able to liquidate the shares should there be a need or desire to do so.

Market volatility may affect our stock price and the value of your investment.

The market price for our common stock, similar to other biopharmaceutical companies, is likely to be volatile. The market price of our common stock may fluctuate significantly in response to a number of factors, most of which we cannot control, including, among others:

plans for, progress of or results from non-clinical and clinical development activities related to our product candidates;

the failure of the FDA to approve our product candidates;

announcements of new products, technologies, commercial relationships, acquisitions or other events by us or our competitors;

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the success or failure of other CNS therapies;

regulatory or legal developments in the United States and other countries;

failure of our product candidates, if approved, to achieve commercial success;

fluctuations in stock market prices and trading volumes of similar companies;

general market conditions and overall fluctuations in U.S. equity markets;

variations in our quarterly operating results;

changes in our financial guidance or securities analysts' estimates of our financial performance;

changes in accounting principles;

our ability to raise additional capital and the terms on which we can raise it;

sales of large blocks of our common stock, including sales by our executive officers, directors and significant stockholders;

additions or departures of key personnel;

discussion of us or our stock price by the press and by online investor communities; and

other risks and uncertainties described in these risk factors.

Future sales and issuances of our common stock may cause our stock price to decline.

Sales or issuances of a substantial number of shares of our common stock in the public market, or the perception that these sales or issuances are occurring or might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

The stock market in general, and small biopharmaceutical companies like ours in particular, have frequently experienced volatility in the market prices for securities that often has been unrelated to the operating performance of the underlying companies. These broad market and industry fluctuations may adversely affect the market price of our common stock, regardless of our operating performance. In certain recent situations in which the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against such company that issued the stock. If any of our stockholders were to bring a lawsuit against us, the defense and disposition of the lawsuit could be costly and divert the time and attention of our management and harm our operating results. Additionally, if the trading volume of our common stock remains low and limited there will be an increased level of volatility and you may not be able to generate a return on your investment.

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future. Future sales of shares by existing stockholders could cause our stock price to decline, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Historically, there has been a limited public market for shares of our common stock. Future sales and issuances of a substantial number of shares of our common stock in the public market, including shares issued upon the conversion of our Series A Preferred, Series B Preferred or Series C Preferred, and the exercise of outstanding options and warrants for common stock which are issuable upon exercise, in the public market, or the perception that these sales and issuances are occurring or might occur, could significantly reduce the market price for our common stock and impair our ability to raise adequate capital through the sale of equity securities.

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Our principal institutional stockholders may continue to have substantial control over us and could limit your ability to influence the outcome of key transactions, including changes in control.

Certain of our current institutional stockholders own a substantial portion of our outstanding capital stock, including our common stock, Series A Preferred, Series B Preferred, and Series C Preferred, all of which preferred stock is convertible into a substantial number of shares of common stock. Accordingly, institutional stockholders may exert significant influence over us and over the outcome of any corporate actions requiring approval of holders of our common stock, including the election of directors and amendments to our organizational documents, such as increases in our authorized shares of common stock, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions. These stockholders may also delay or prevent a change of control of us, even if such a change of control would benefit our other stockholders. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise. Furthermore, the interests of our principal institutional stockholders may not always coincide with your interests or the interests of other stockholders may act in a manner that advances its best interests and not necessarily those of other stockholders, including seeking a premium value for its common stock, which might affect the prevailing market price for our common stock.

If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our common stock, the price of our common stock could decline.

The trading market for our common stock relies in part on the research and reports that equity research analysts publish about us and our business. We do not control these analysts. The price of our common stock could decline if one or more equity research analysts downgrade our common stock or if analysts issue other unfavorable commentary or cease publishing reports about us or our business.

There may be additional issuances of shares of preferred stock in the future.

Our Restated Articles of Incorporation (the Articles) permit us to issue up to 10.0 million shares of preferred stock. Our Board of Directors has authorized the issuance of (i) 500,000 shares of Series A Preferred, all of which shares are issued and outstanding at June 30, 2017; (ii) 4.0 million shares of Series B 10% Convertible Preferred stock, of which approximately 1.2 million shares remain issued and outstanding at June 30, 2017; and (iii) 3.0 million shares of Series C Convertible Preferred Stock, of which approximately 2.3 million shares are issued and outstanding at June 30, 2017. Our Board of Directors could authorize the issuance of additional series of preferred stock in the future and such preferred stock could grant holders preferred rights to our assets upon liquidation, the right to receive dividends before dividends would be declared to holders of our common stock, and the right to the redemption of such shares, possibly together with a premium, prior to the redemption of the common stock. In the event and to the extent that we do issue additional preferred stock in the future, the rights of holders of our common stock could be impaired thereby, including without limitation, with respect to liquidation.

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

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

We incur significant costs to ensure compliance with corporate governance, federal securities law and accounting requirements.

Since becoming a public company by means of a reverse merger in 2011, we have been subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (Exchange Act), which requires that we file annual, quarterly and current reports with respect to our business and financial condition, and the rules and regulations implemented by the SEC, the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act, and the Public Company Accounting Oversight Board, each of which imposes additional reporting and other obligations on public companies. We have incurred and will continue to incur significant costs to comply with these public company reporting requirements, including accounting and related audit costs, legal costs to comply with corporate governance requirements and other costs of operating as a public company. These legal and financial compliance costs will continue to require us to divert a significant amount of money that we could otherwise use to achieve our research and development and other strategic objectives.

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The filing and internal control reporting requirements imposed by federal securities laws, rules and regulations on companies that are not “smaller reporting companies” under federal securities laws are rigorous and, once we are no longer a smaller reporting company, we may not be able to meet them, resulting in a possible decline in the price of our common stock and our inability to obtain future financing. Certain of these requirements may require us to carry out activities we have not done previously and complying with such requirements may divert management’s attention from other business concerns, which could have a material adverse effect on our business, results of operations, financial condition and cash flows. Any failure to adequately comply with applicable federal securities laws, rules or regulations could subject us to fines or regulatory actions, which may materially adversely affect our business, results of operations and financial condition.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We will continue to invest resources to comply with evolving laws, regulations and standards, however this investment may result in increased general and administrative expenses and a diversion of management’s time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business may be adversely affected.

Risks Related to this Offering

Our management team may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return.

Our management will have broad discretion over the use of proceeds from this offering. We currently intend to use the net proceeds from the sale of securities offered by this prospectus for general corporate purposes, including research and development, working capital and capital expenditures. We may use a portion of the net proceeds to fund production of, and nonclinical and clinical studies related to Phase 2 and Phase 3 development of, AV-101 and other drug candidates. We may also use the net proceeds from the sale of the securities under this prospectus to in-license, acquire or invest in complementary businesses, technologies, products or assets. However, our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates.

Purchasers in this offering will experience immediate and substantial dilution in the book value of their investment.

Because the combined public offering price per share and related Warrants is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. After giving effect to the sale by us of 1,371,430 shares of our common stock and Warrants to purchase up to an aggregate total of 1,892,572 shares of common stock in this offering at a combined public offering price of \$1.75 per share and related Warrants, and after deducting the underwriting discount and estimated offering expenses payable by us and attributing no value to the Warrants sold in this offering, you will suffer immediate and substantial dilution of \$1.62 per share in the net tangible book value of the common stock you

purchase in this offering. To the extent outstanding options, warrants or other derivative securities are ultimately exercised or converted, or if we issue restricted stock to our employees under our equity incentive plans, there will be further dilution to investors who purchase shares in this offering. In addition, if we issue additional equity securities or derivative securities, investors purchasing shares in this offering will experience additional dilution. For a further description of the dilution that you will experience immediately after this offering, see “Dilution” on page S-43.

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Sales of a substantial number of shares of our common stock, or the perception that such sales may occur, may adversely impact the price of our common stock.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception that such sales may occur, may adversely impact the price of our common stock, even if there is no relationship between such sales and the performance of our business. As of August 31, 2017, we have 9,380,041 shares of common stock outstanding, as well as outstanding options to purchase an aggregate of 2,509,871 shares of our common stock at a weighted average exercise price of \$3.74 per share, up to 4,228,252 shares of common stock issuable upon conversion of outstanding shares of our preferred stock and outstanding warrants to purchase up to an aggregate of 4,825,078 shares of our common stock at a weighted average exercise price of \$6.17 per share. The exercise of such outstanding derivative securities may result in further dilution of your investment.

There is no public market for the Warrants being offered by this prospectus supplement and the accompanying prospectus, and we do not anticipate such a market ever developing in the future.

There is no established public trading market for the Warrants being offered by this prospectus supplement and the accompanying prospectus and we do not intend to have the Warrants listed on a national securities exchange or any other recognized trading system in the future. Without an active market, the liquidity of any Warrants sold by means of this prospectus supplement and the accompanying prospectus will be limited.

The Warrants being offered by means of this prospectus supplement and the accompanying prospectus may not have any value.

The Warrants offered by us in this offering do not confer any rights of ownership of shares of common stock on its holders, such as voting rights or the right to receive dividends, but only represent the right to acquire shares of common stock at a fixed price for a limited period of time. In the event that the market price of our common stock does not exceed the exercise price of the Warrants sold in this offering during the period when the Warrants are exercisable, the Warrants may not have any value.

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CAUTIONARY NOTES REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this prospectus supplement and the accompanying prospectus, other than statements of historical facts, are forward-looking statements including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth. These statements involve known and unknown risks, uncertainties and other important 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 the forward-looking statements.

The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “warrant,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

the availability of capital to satisfy our working capital requirements;

the accuracy of our estimates regarding expenses, future revenues and capital requirements;

our plans to develop and commercialize our lead product candidate, AV-101, initially as an adjunctive treatment for MDD in patients with an inadequate response to standard, FDA-approved antidepressants, and subsequently as a treatment for additional CNS diseases and disorders;

our ability to initiate and complete our clinical trials and to advance our product candidates into additional clinical trials, including pivotal clinical trials, and successfully complete such clinical trials;

regulatory developments in the U.S. and foreign countries;

the performance of the U.S. National Institute of Mental Health, our third-party contractors involved with the manufacturer and production of our drug candidates for nonclinical and clinical development activities, contract research organizations and other third-party nonclinical and clinical development collaborators and regulatory service providers;

our ability to obtain and maintain intellectual property protection for our core assets;

the size of the potential markets for our product candidates and our ability to serve those markets;

the rate and degree of market acceptance of our product candidates for any indication once approved;

the success of competing products and product candidates in development by others that are or become available for the indications that we are pursuing;

the loss of key scientific, clinical and nonclinical development, and/or management personnel, internally or from one of our third-party collaborators; and

other risks and uncertainties, including those described under Item 1A, "Risk Factors," in our Annual Report on Form 10-K for the fiscal year ended March 31, 2017 and subsequent Quarterly Reports on Form 10-Q, which risk factors are incorporated herein by reference.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this prospectus supplement, as well as certain information incorporated by reference into this prospectus supplement and the accompanying prospectus, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus supplement and the accompanying prospectus with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately \$2.0 million, after deducting the underwriting discount and estimated offering expenses payable by us.

We currently intend to use the net proceeds from the sale of the securities offered by this prospectus supplement for general corporate purposes, including research and development related to preparations for our planned AV-101 MDD Phase 2 Adjunctive Treatment Study, and working capital.

The table below reflects our current planned use of the net proceeds from this offering, assuming no exercise of the Warrants. Each of these amounts is an estimate only, and is subject to change at any time before or after closing of the offering.

	Amounts in \$000
Gross proceeds	\$2,400
Underwriting discount, and other expenses of the offering	\$(369)
Net proceeds	\$2,031
Research and development:	
Operations	\$405
Preparation for our AV-101 MDD Phase 2 Adjunctive Treatment Study	\$927
Total research and development	\$1,332
General and administrative, working capital and other general corporate purposes	\$699
	\$2,031

Although we expect net proceeds from this offering to provide sufficient funding to complete preparations for our AV-101 MDD Phase 2 Adjunctive Treatment Study, the net proceeds from this offering will not be sufficient to launch the study. Assuming no exercise of the Warrants issued in this offering, we believe an additional \$15 million to \$20 million will be required prior to the launch of the AV-101 MDD Phase 2 Adjunctive Treatment Study in the first quarter of 2018 to complete the study as proposed in the fourth quarter of 2018. No assurances can be provided that such additional capital will be available to us when necessary, on reasonable terms, or at all. In the event we are unable to raise such additional capital, our operations will be negatively and materially affected.

Pending other uses, we intend to invest our proceeds from the offering in short-term investments or hold them as cash. We cannot predict whether the proceeds invested will yield a favorable return. Our management will have broad discretion in the use of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds.

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DILUTION

If you purchase shares of our common stock in this offering, you will experience dilution to the extent of the difference between the combined public offering price per share and related Warrants in this offering and our as adjusted net tangible book value per share immediately after this offering assuming no value is attributed to the Warrants, and such Warrants are accounted for and classified as equity. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding. As of June 30, 2017, our net tangible book value was approximately \$(606,800), or approximately \$(0.07) per share.

After giving effect to the sale by us of 1,371,430 shares of common stock and Warrants to purchase 1,892,572 shares of our common stock in this offering at a combined public offering price of \$1.75 per share and related Warrants, and after deducting the underwriting discount and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2017 would have been approximately \$1.4 million, or approximately \$0.13 per share. This amount represents an immediate increase in net tangible book value of \$0.20 per share to existing stockholders and an immediate dilution in net tangible book value of \$1.62 per share to purchasers of our common stock and related Warrants in this offering.

The following table illustrates the dilution in net tangible book value per share to new investors:

Public offering price per share and related Warrants:	\$1.75
Net tangible book value per share as of June 30, 2017	\$(0.07)
Increase in net tangible book value per share after this offering	\$0.20
Net tangible book value per share after this offering	\$0.13
Dilution per share to new investors	\$1.62

The foregoing discussion and table do not take into account further dilution to new investors that could occur upon the exercise of outstanding options or warrants having a per share exercise price less than the combined public offering price in this offering. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the issuance of those securities could result in further dilution to our stockholders.

The number of shares of our common stock that will be outstanding immediately after the offering is based on 9,301,472 shares outstanding as of June 30, 2017, and excludes:

2,522,593 shares of common stock reserved for issuance upon exercise of outstanding stock options under our 1999 Stock Incentive Plan and our Amended and Restated 2016 Stock Incentive Plan, with a weighted average exercise price of \$3.77 per share;

312,407 shares of common stock reserved for future issuance in connection with future grants under our Amended and Restated 2016 Stock Incentive Plan;

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4,796,506 shares of common stock that have been reserved for issuance upon exercise of outstanding warrants, with a weighted average exercise price of \$6.19 per share;

750,000 shares of common stock reserved for issuance upon conversion of 500,000 shares our Series A Preferred;

1,160,240 shares of common stock reserved for issuance upon conversion of 1,160,240 shares of our Series B Preferred and 663,460 shares of common stock for issuance as payment of accrued dividends on outstanding shares of Series B Preferred;

2,318,012 shares of common stock reserved for issuance upon conversion of 2,318,012 shares of our Series C Preferred; and

1,892,572 shares of common stock issuable upon the exercise of the Warrants offered hereby.

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DESCRIPTION OF SECURITIES WE ARE OFFERING

Common stock

The material terms and provisions of our common stock are described under the caption “Description of our Capital Stock” in the accompanying prospectus beginning on page 9. As of August 31, 2017, we had 9,380,044 shares of our common stock outstanding. Our common stock is listed on the NASDAQ Capital Market under the symbol “VTGN”.

Warrants

Duration and Exercise Price: By means of this prospectus supplement, we are offering Series A-1 Warrants to purchase up to 1,388,931 shares of Common Stock and Series A2 Warrants to purchase up to 503,641 shares of Common Stock. Each Series A1 Warrant will be exercisable for a five-year period commencing on March 7, 2018. Each Series A2 Warrant will be exercisable for a five-year period commencing on the date of issuance.

Exercisability: Each of the Warrants may be exercised, in whole or in part, by delivering to the Company a written notice of election to exercise the applicable Warrant and delivering to the Company cash payment of the exercise price, if applicable. The exercise price and the number of shares of our common stock issuable upon exercise of the Warrants is subject to adjustment in the event of certain subdivisions and combinations, including by any stock split or reverse stock split, stock dividend, recapitalization or otherwise. In addition, the Company has the right at any time during the term of the Warrants to reduce the then-existing exercise price to any amount and for any period of time deemed appropriate by our Board of Directors.

Cashless Exercise: If, at any time during the term of the Warrants, the issuance or resale of shares of our common stock upon exercise of the Warrants is not covered by an effective registration statement, the holder is permitted to effect a cashless exercise of the Warrants (in whole or in part) in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the Warrants. Shares issued pursuant to a cashless exercise would be deemed to have been issued pursuant to the exemption from registration provided by Section 3(a)(9) of the Securities Act of 1933, and amended (the Securities Act), and the shares of common stock issued upon such cashless exercise would take on the characteristics of the Warrants being exercised, including, for purposes of Rule 144(d) promulgated under the Securities Act, a holding period beginning from the original issuance date of the Warrants.

Adjustment Provisions: The exercise price and the number and type of securities purchasable upon exercise of the Warrants are subject to adjustment upon certain corporate events, including certain subdivisions, combinations and similar events. If we declare any dividend or distribution of assets (including cash, stock or other securities, evidence of indebtedness, purchase rights or other property), each holder of a Warrant will be entitled to participate in such distribution to the same extent that the holder would have participated had the applicable Warrant been exercised immediately before the record date for the distribution. In addition, the Series A2 Warrants contain full ratchet anti-dilution protection upon the issuance of any common stock, securities convertible into common stock or certain other issuances at a price below the then-existing exercise price of the Warrants, with certain exceptions; provided, however, that such anti-dilution protection will terminate once the Company has raised through the issuance of common stock or equity-linked securities at least \$20 million in gross proceeds in the aggregate. In addition, the Company has the right at any time during the term of the Warrants to reduce the then-existing exercise price to any amount and for any period of time deemed appropriate by our Board of Directors. The terms of the Warrants, including the anti-dilution protections in the Series A2 Warrant described above, may make it difficult for us to raise additional capital at prevailing market terms in the future.

Transferability: Subject to applicable laws, the Warrants may be offered for sale, sold, transferred or assigned without our consent. However, as of the date of this prospectus supplement there is no established trading market for the Warrants and it is not expected that a trading market for the Warrants will develop in the future. Without an active trading market, the liquidity of the Warrants will be limited.

Listing: We will not apply to list the Warrants on NASDAQ Capital Market. We do not intend to list the Warrants on any securities exchange or other quotation system. Without an active market, the liquidity of the Warrants will be limited.

Rights as a stockholder: Except as set forth in the Warrants or by virtue of such holders' ownership of shares of our common stock, the holders of the Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise the Warrants.

Limitations on Exercise: The exercise of the Warrants may be limited in certain circumstances if, after giving effect to such exercise, the holder or any of its affiliates would beneficially own (as determined in accordance with the terms of the Warrants) more than 4.99% (or, at the election of the holder, 9.99%) of our outstanding common stock immediately after giving effect to the exercise.

Fundamental Transactions: In the event of certain fundamental transactions, as described in the Warrants and generally including any merger or consolidation with or into another entity, the holders of the Warrants shall thereafter have the right to exercise the applicable Warrant for the same amount and kind of securities, cash or property as it would have been entitled to receive upon the occurrence of such fundamental transaction if it had been, immediately prior to such fundamental transaction, the holder of shares of common stock issuable upon exercise in full of the Warrant. In the event of a Change of Control (as defined in the Warrants) (other than a Change of Control which was not approved by the Board of Directors, as to which this right shall not apply), at the request of the holder delivered before the 30th day after such Change of Control, a holder of a Warrant will have the right to require us or any successor entity to purchase the holder's Warrant for the Black-Scholes Value of the remaining unexercised portion of the Warrant on the effective date of such Change of Control (determined in accordance with a formula specified in the Warrants), payable in cash; provided, that if the applicable Change of Control was not approved by our Board of Directors, such amount shall be payable, at our option in either (x) shares of our common stock or the consideration receivable by holders of common stock in the Change of Control transaction, as applicable, valued at the value of the consideration received by the shareholders in such Change of Control, or (y) cash.

Dividends and Other Distributions: If we declare or make any dividend or other distribution of our assets to holders of shares of our common stock (including any distribution of cash, stock or other securities, property, options, evidence of indebtedness or any other assets), then, subject to certain limitation on exercise described in the Warrants, each holder of a Warrant shall receive the distributed assets that such holder would have been entitled to receive in the distribution had the holder exercised the Warrant immediately prior to the record date for the distribution.

The foregoing summary of certain terms and provisions of the Warrants that are being offered hereby is not complete and is subject to, and is qualified in its entirety by the provisions of the form of the Warrants filed as exhibits to our Current Report on Form 8-K filed in connection with this offering. Prospective investors should carefully review the terms and provisions of the warrant agreements and forms of the Warrants for a complete description of the terms and conditions of the Warrants.

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UNDERWRITING

We have entered into an underwriting agreement with Oppenheimer & Co. Inc. on August 31, 2017. Oppenheimer & Co. Inc. is acting as the sole underwriter for this offering. The underwriting agreement provides for the purchase of a specific number of shares of common stock and related Series A1 and Series A2 Warrants by the underwriter.

Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriter, and the underwriter has agreed to purchase, at the public offering price less the underwriting discount set forth on the cover page of this prospectus supplement, the number of shares of common stock and the related Warrants listed next to its name in the following table:

Name	Number of Shares	Number of Series A1 Warrants	Number of Series A2 Warrants
Oppenheimer & Co. Inc.	1,371,430	1,388,931	503,641
Total	1,371,430	1,388,931	503,641

The underwriter is committed to purchase all the shares of common stock and the related Warrants offered by us if it purchases any such securities.

The underwriter proposes to offer the shares of common stock and the related Warrants directly to the public at the public offering price set forth on the cover page of this prospectus supplement. After the public offering of the securities, the offering price and other selling terms may be changed by the underwriter.

The following table shows the underwriting discount to be paid to the underwriter in connection with this offering.

	Per Share of Common Stock and Related Warrants	Total
Public offering price	\$1.75	\$2,400,002.50
Underwriting discount	\$0.1225	\$168,000.175

We estimate that our total expenses of the offering, including the estimated underwriting discount, will be approximately \$400,000, which includes the costs and expenses for which we have agreed to reimburse the underwriters for certain expenses, including for fees and expenses of its legal counsel up to an amount of \$85,000, provided that any such costs and expenses may not exceed \$105,000 in the aggregate.

Subject to certain exceptions, for a period through September 30, 2018, we have agreed not to negotiate with any other underwriter or placement agent relating to a possible public or private offering or placement of our securities or other financing without first consulting and receiving the approval of the underwriter.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

We have agreed to a 75-day “lock-up” and our officers and directors have agreed to a 90-day “lock-up” with respect to shares of our common stock and other of our securities that they beneficially own, including securities that are convertible into shares of common stock and securities that are exchangeable or exercisable for shares of common stock. This means that, subject to certain exceptions, for a period of 75 days following the date of the prospectus

supplement, we may not, and for a period of 90 days following the date of this prospectus supplement, such persons may not offer, sell, pledge or otherwise dispose of these securities without the prior written consent of Oppenheimer & Co. Inc.

The underwriter has advised us that it does not intend to conduct any stabilization or over-allotment activities in connection with this offering.

Electronic Delivery of Preliminary Prospectus Supplement: A prospectus supplement in electronic format may be delivered to potential investors by one or more of the underwriters participating in this offering. The prospectus supplement in electronic format will be identical to the paper version of such preliminary prospectus supplement. Other than the prospectus supplement in electronic format, the information on any underwriter's website and any information contained in any other website maintained by an underwriter is not part of this prospectus supplement, the accompanying prospectus or the registration statement of which this prospectus supplement and the accompanying prospectus forms a part.

The underwriter and its affiliates have provided in the past and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and our affiliates in the ordinary course of their business, for which they may receive customary fees and commissions. In addition, from time to time, the underwriter and its affiliates may effect transactions for their own accounts or the accounts of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

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NOTICE TO INVESTORS

Offer Restrictions Outside the United States

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any securities which are the subject of the offering contemplated by this prospectus supplement may not be made in that Relevant Member State other than the offers contemplated in this prospectus supplement in name(s) of Member State(s) where prospectus will be approved or passported for the purposes of a non-exempt offer once this prospectus supplement has been approved by the competent authority in such Member State and published and passported in accordance with the Prospectus Directive as implemented in name(s) of relevant Member State(s) except that an offer to the public in that Relevant Member State of any securities may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) by the representative to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive); or
- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of securities shall result in a requirement for the publication by the Company or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer to the public” in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any securities to be offered so as to enable an investor to decide to purchase any securities, as the same may

be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

United Kingdom

The underwriter has represented, warranted and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000 (the FSMA)) received by it in connection with the issue or sale of any securities in circumstances in which section 21(1) of the FSMA does not apply to the Company; and
- (b) it has complied with and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom

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Israel

In the State of Israel, the securities offered hereby may not be offered to any person or entity other than the following:

- (a) a fund for joint investments in trust (i.e., mutual fund), as such term is defined in the Law for Joint Investments in Trust, 5754-1994, or a management company of such a fund;
- (b) a provident fund as defined in Section 47(a)(2) of the Income Tax Ordinance of the State of Israel, or a management company of such a fund;
- (c) an insurer, as defined in the Law for Oversight of Insurance Transactions, 5741-1981, (d) a banking entity or satellite entity, as such terms are defined in the Banking Law (Licensing), 5741-1981, other than a joint services company, acting for their own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (d) a company that is licensed as a portfolio manager, as such term is defined in Section 8(b) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (e) a company that is licensed as an investment advisor, as such term is defined in Section 7(c) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account;
- (f) a company that is a member of the Tel Aviv Stock Exchange, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (g) an underwriter fulfilling the conditions of Section 56(c) of the Securities Law, 5728-1968;
- (h) a venture capital fund (defined as an entity primarily involved in investments in companies which, at the time of investment, (i) are primarily engaged in research and development or manufacture of new technological products or processes and (ii) involve above-average risk);
- (i) an entity primarily engaged in capital markets activities in which all of the equity owners meet one or more of the above criteria; and
- (j) an entity, other than an entity formed for the purpose of purchasing securities in this offering, in which the shareholders equity (including pursuant to foreign accounting rules, international accounting regulations and U.S. generally accepted accounting rules, as defined in the Securities Law Regulations (Preparation of Annual Financial Statements), 1993) is in excess of NIS 50 million.

Any offeree of the securities offered hereby in the State of Israel shall be required to submit written confirmation that it falls within the scope of one of the above criteria. This prospectus supplement will not be distributed or directed to investors in the State of Israel who do not fall within one of the above criteria.

In Canada

The securities subject to this offering are not qualified for sale in Canada and may not be offered or sold in Canada, directly or indirectly, on our behalf.

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LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Disclosure Law Group, a Professional Corporation, San Diego, California (DLG). Partners of DLG beneficially own an aggregate of 65,987 registered and/or restricted shares of our common stock. Lowenstein Sandler LLP, New York, New York, is acting as counsel for the underwriter in connection with this offering.

EXPERTS

The financial statements of the Company incorporated in this prospectus by reference to the Annual Report on Form 10-K for the fiscal year ended March 31, 2017 have been audited by OUM & Co. LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference room at 100 F Street, NE, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available, at no charge, to the public at the SEC's website at <http://www.sec.gov>.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The following documents filed by us with the SEC are incorporated by reference in this prospectus:

Annual Report on Form 10-K for the fiscal year ended March 31, 2017, filed on June 29, 2017;

Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, filed on August 14, 2017;

Current Reports on Form 8-K, filed on April 28, 2017, May 1, 2017, June 29, 2017, August 9, 2017, August 14, 2017 and August 31, 2017; and

The description of our common stock contained in the Registration Statement on Form 8-A filed pursuant to Section 12(b) of the Exchange Act on May 3, 2016, including any amendment or report filed with the SEC for the purpose of updating this description.

We also incorporate by reference all documents we file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than any portions of filings that are furnished rather than filed pursuant to Items 2.02 and 7.01 of a Current Report on Form 8-K) after the date of the initial registration statement of which this prospectus is a part and prior to effectiveness of such registration statement. All documents we file in the future pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of the offering are also incorporated by reference and are an important part of this prospectus.

Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for the purposes of this registration statement to the extent that a statement contained herein or in any other subsequently filed document which also is or deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this registration statement.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of this prospectus supplement and any or all of the information that has been incorporated by reference in the prospectus supplement but not delivered herewith. You may request a copy of these filings, excluding the exhibits to such filings which we have not specifically incorporated by reference in such filings, at no cost, by writing to or calling us at:

VistaGen Therapeutics, Inc.
Attn: Corporate Secretary
343 Allerton Avenue
South San Francisco, CA 94080
(650) 577-3600

Except for the specific incorporated documents listed above, no information available on or through our website shall be deemed to be incorporated in this prospectus supplement or the accompanying prospectus.

BASE PROSPECTUS

\$100,000,000

Common Stock
Preferred Stock
Warrants
Units

From time to time, we may offer and sell, in one or more offerings, up to \$100,000,000 of any combination of the securities described in this prospectus. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable anti-dilution provisions.

This prospectus provides a general description of the securities we may offer from time to time. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with an offering. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

Our common stock is quoted on The NASDAQ Capital Market under the symbol "VTGN". The last reported sale price of our common stock on March 31, 2017 was \$1.96 per share.

We may offer and sell our securities to or through one or more agents, underwriters, dealers or other third parties or directly to one or more purchasers on a continuous or delayed basis. If agents, underwriters or dealers are used to sell our securities, we will name them and describe their compensation in a prospectus supplement. The price to the public of our securities and the net proceeds we expect to receive from the sale of such securities will also be set forth in a prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus.

As of January 10, 2017, the aggregate market value of our outstanding common stock held by non-affiliates was approximately \$31.4 million, which was calculated based on 8,543,137 shares of outstanding common stock held by non-affiliates, at a price per share of \$3.68. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell the securities described in this prospectus in a public primary offering with a value exceeding more than one-third (1/3) of the aggregate market value of our common stock held by non-affiliates in any twelve (12)-month period, so long as the aggregate market value of our outstanding common stock held by non-affiliates remains below \$75 million. During the twelve (12) calendar months prior to and including the date of this prospectus, we have not offered or sold any securities pursuant to General Instruction I.B.6 of Form S-3.

Our business and investing in our securities involves significant risks. You should review carefully the risks and uncertainties referenced under the heading "Risk Factors" on page 5 of this prospectus, as well as those contained in the applicable prospectus supplement and any related free writing prospectus, and in the other documents that are

incorporated by reference into this prospectus or the applicable prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 27, 2017

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement filed with the Securities and Exchange Commission (the SEC), using a “shelf” registration process. Under this shelf registration process, we may sell the securities described in this prospectus in one or more offerings. This prospectus provides you with a general description of the securities which may be offered. Each time we offer securities for sale, we will provide a prospectus supplement that contains information about the specific terms of that offering. Any prospectus supplement may also add or update information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described below under “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.”

You should rely only on the information contained or incorporated by reference in this prospectus, and in any prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making offers to sell or solicitations to buy the securities described in this prospectus in any jurisdiction in which an offer or solicitation is not authorized, or in which the person making that offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make an offer or solicitation. You should not assume that the information in this prospectus or any prospectus supplement, as well as the information we file or previously filed with the SEC that we incorporate by reference in this prospectus or any prospectus supplement, is accurate as of any date other than its respective date. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find More Information”.

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COMPANY OVERVIEW

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all the information you should consider before buying our common stock. You should read the following summary together with the more detailed information appearing in this prospectus, including the section titled “Risk Factors” on page 5, before deciding whether to purchase our securities.

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to “VistaGen,” the “Company,” “we,” “us,” and “our” refer to VistaGen Therapeutics, Inc., a Nevada corporation.

Overview

We are a clinical-stage biopharmaceutical company focused on developing new generation medicines for depression and other central nervous system (CNS) disorders.

AV-101, our lead CNS product candidate, is a new generation oral antidepressant prodrug candidate in Phase 2 development as an adjunctive treatment for Major Depressive Disorder (MDD) in patients with an inadequate response to standard antidepressants approved by the U.S. Food and Drug Administration (FDA). We believe AV-101 may also have the potential to treat multiple additional CNS diseases and disorders, including chronic neuropathic pain, epilepsy, Huntington’s disease and Parkinson’s disease. AV-101’s mechanism of action, as an N-methyl D aspartate receptor (NMDAR) antagonist binding selectively at the glycine binding (GlyB) co-agonist site of the NMDAR, is fundamentally differentiated from all FDA-approved antidepressants currently on the market, as well as all atypical antipsychotics used as adjunctive treatments with current antidepressants.

Clinical studies conducted at the U.S. National Institute of Mental Health (NIMH), part of the U.S. National Institutes of Health (NIH), by Dr. Carlos Zarate, Jr., Chief of the NIMH’s Experimental Therapeutics & Pathophysiology Branch and its Section on Neurobiology and Treatment of Mood and Anxiety Disorders, have focused on the antidepressant effects of low dose intravenous (IV) administration of ketamine hydrochloride (ketamine), an NMDAR antagonist, in patients with treatment-resistant MDD. These NIMH studies, as well as clinical research at Yale University and other academic institutions, have demonstrated robust antidepressant effects in treatment-resistant MDD patients within twenty-four hours of a single IV dose of ketamine.

As published in the October 2015 issue of the peer-reviewed, Journal of Pharmacology and Experimental Therapeutics, in an article entitled, The prodrug 4-chlorokynurenine causes ketamine-like antidepressant effects, but not side effects, by NMDA/glycineB-site inhibition, using well-established preclinical models of depression, AV-101 was shown to induce fast-acting, dose-dependent, persistent and statistically significant antidepressant-like responses following a single treatment. These responses were equivalent to those seen with a single sub-anesthetic control dose of ketamine. In addition, these studies confirmed that the fast-acting antidepressant effects of AV-101 were mediated through the GlyB site and also involved the activation of another key neurological pathway, the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor pathway

In February 2015, we entered into a Cooperative Research and Development Agreement (CRADA) with the NIMH. Under the CRADA, the NIMH is funding, and Dr. Zarate, as Principal Investigator, and his team are conducting, a 20-25 patient Phase 2 clinical study of AV-101 as a monotherapy in subjects with treatment-resistant MDD (the NIMH Study). We believe orally-administered AV-101 may have potential to deliver ketamine-like antidepressant effects without ketamine’s psychological and other side effects. We currently anticipate that the NIMH

will complete the NIMH Study at the end of 2017.

We are preparing to launch our Phase 2 clinical study of AV-101 as a new generation adjunctive treatment of MDD in adult patients with an inadequate response to standard, FDA-approved antidepressants (Phase 2 Study). We currently anticipate commencement of this multi-center, multi-dose, double blind, placebo-controlled efficacy and safety study of AV-101 by the end of the second quarter of 2017. Dr. Maurizio Fava, Professor of Psychiatry at Harvard Medical School and Director, Division of Clinical Research, Massachusetts General Hospital (MGH) Research Institute, will be the Principal Investigator of the Phase 2 Study. Dr. Fava was the co-Principal Investigator with Dr. A. John Rush of the STAR*D study, the largest clinical trial conducted in depression to date, whose findings were published in journals such as the New England Journal of Medicine (NEJM) and the Journal of the American Medical Association (JAMA). We currently anticipate top line results of the Phase 2 Study by the end of 2018.

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VistaStem Therapeutics (VistaStem) is our wholly owned subsidiary focused on applying human pluripotent stem cell (hPSC) technology, internally and with third-party collaborators, to discover, rescue, develop and commercialize (i) proprietary new chemical entities (NCEs), including small molecule NCEs with regenerative potential, for CNS and other diseases and (ii) cellular therapies involving stem cell-derived blood, cartilage, heart and liver cells. Our internal drug rescue programs are designed to utilize CardioSafe 3D, our customized cardiac bioassay system, to develop small molecule NCEs for our pipeline. In December 2016, we exclusively sublicensed to BlueRock Therapeutics LP, a next generation regenerative medicine company established by Bayer AG and Versant Ventures, rights to certain proprietary technologies relating to the production of cardiac stem cells for the treatment of heart disease (the BlueRock Agreement). VistaStem may also pursue additional potential regenerative medicine (RM) applications, including using blood, cartilage, and/or liver cells derived from hPSCs for (A) cell-based therapy, (B) cell repair therapy, and/or (C) tissue engineering. In a manner similar to our exclusive sublicense agreement with BlueRock Therapeutics, VistaStem may pursue these additional RM applications in collaboration with third-parties.

AV-101 and Major Depressive Disorder

Background

The World Health Organization (WHO) estimates that 300 million people worldwide are affected by depression. According to the NIH, major depression is one of the most common mental disorders in the U.S. The NIMH reports that, in 2014, an estimated 15.7 million adults aged 18 or older in the U.S. had at least one major depressive episode in the past year. This represented 6.7 percent of all U.S. adults. According to the U.S. Centers for Disease Control and Prevention (CDC) one in 10 Americans over the age of 12 takes a standard, FDA-approved antidepressant.

Most standard, FDA-approved antidepressants target neurotransmitter reuptake inhibition – either serotonin (antidepressants known as SSRIs) or serotonin/norepinephrine (antidepressants known as SNRIs). Even when effective, these standard depression medications take many weeks to achieve adequate antidepressant effects. Nearly two out of every three drug-treated depression patients, including an estimated 6.9 million drug-treated MDD patients in the U.S., obtain inadequate therapeutic benefit from initial treatment with a standard antidepressant. Unfortunately, even after treatment with many different standard antidepressants, nearly one out of every three drug-treated depression patients still do not achieve adequate therapeutic benefits from their antidepressant medication. Such patients with an inadequate response to standard antidepressants often seek to augment their treatment regimen by adding an atypical antipsychotic (drugs such as, for example, aripiprazole), despite only modest potential therapeutic benefit and the risk of additional side effects from atypical antipsychotics.

All standard, FDA-approved antidepressants have risks of significant side effects, including, among others, potential anxiety, metabolic syndrome, sleep disturbance and sexual dysfunction. Adjunctive use of atypical antipsychotics to augment inadequately performing standard antidepressants increases the risk of serious side effects, including, potentially, tardive dyskinesia, significant weight gain, diabetes and heart disease, while offering only a modest potential increase in therapeutic benefit.

AV-101

AV-101 is our oral new generation antidepressant prodrug candidate in Phase 2 clinical development in the U.S. for the adjunctive treatment of MDD patients with an inadequate response to standard, FDA-approved antidepressants. As published in the October 2015 issue of the peer-reviewed, Journal of Pharmacology and Experimental Therapeutics, in an article entitled, The prodrug 4-chlorokynurenine causes ketamine-like antidepressant effects, but not side effects, by NMDA/glycineB-site inhibition, using well-established preclinical models of depression, AV-101 was shown to induce fast-acting, dose-dependent, persistent and statistically significant antidepressant-like responses following a

single treatment. These responses were equivalent to those seen with a single sub-anesthetic control dose of ketamine. In addition, these studies confirmed that the fast-acting antidepressant effects of AV-101 were mediated through the GlyB site and also involved the activation of another key neurological pathway, the alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor pathway. We believe activation of the AMPA receptor pathway is a key final common pathway feature of new generation antidepressants.

Following the completion of our NIH-funded, randomized, double blind, placebo-controlled AV-101 Phase 1 safety studies, in February 2015, we entered into a Cooperative Research and Development Agreement (CRADA) with the NIMH. Under the CRADA, the NIMH is funding, and Dr. Zarate, as Principal Investigator, and his team are conducting, a 20-25 patient Phase 2 clinical study of AV-101 as a monotherapy in subjects with treatment-resistant MDD (NIMH Study). We currently anticipate that the NIMH will complete the NIMH Study by the end of 2017.

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We are preparing to launch our approximately 180-patient Phase 2 Study of AV-101 as an adjunctive treatment of MDD in patients with an inadequate response to standard, FDA-approved antidepressants. We currently anticipate the launch of the Phase 2 Study, with Dr. Maurizio Fava of Harvard Medical School serving as Principal Investigator, by the end of the second quarter of 2017. We currently anticipate top line results of the Phase 2 Study by the end of 2018.

We believe prior preclinical studies support the hypothesis that AV-101 may also have the potential to treat multiple CNS disorders and neurodegenerative diseases in addition to MDD, including chronic neuropathic pain, epilepsy, Parkinson's disease and Huntington's disease, where modulation of the NMDAR, AMPA pathway and/or key active metabolites of AV-101 may achieve therapeutic benefit. However, human clinical studies will be required before this therapeutic potential could be demonstrated. There is no guarantee that human clinical trials would be successful or that the FDA would approve the use of AV-101 for the treatment of one or more of these additional CNS indications.

CardioSafe 3D™; NCE Drug Rescue and Regenerative Medicine

VistaStem Therapeutics is our wholly owned subsidiary focused on applying hPSC technology to discover, rescue, develop and commercialize proprietary small molecule NCEs for CNS and other diseases, as well as potential cellular therapies involving stem cell-derived blood, cartilage, heart and liver cells. CardioSafe 3D™ is our customized in vitro cardiac bioassay system capable of predicting potential human heart toxicity of small molecule NCEs in vitro, long before they are ever tested in animal and human studies. Potential commercial applications of our stem cell technology platform involve (i) using CardioSafe 3D internally for NCE drug discovery and (ii) regenerative medicine (RM) and cellular therapies. Drug rescue involves leveraging substantial prior research and development investments by pharmaceutical companies and others related to public domain NCE programs terminated before FDA approval due to heart toxicity risks. In December 2016, we exclusively sublicensed to BlueRock Therapeutics LP, a next generation RM company established by Bayer AG and Versant Ventures, rights to certain proprietary technologies relating to the production of cardiac stem cells for the treatment of heart disease. We may also pursue additional potential RM applications using blood, cartilage, and/or liver cells derived from hPSCs for (A) cell-based therapy (injection of stem cell-derived mature organ-specific cells obtained through directed differentiation), (B) cell repair therapy (induction of regeneration by biologically active molecules administered alone or produced by infused genetically engineered cells), or (C) tissue engineering (transplantation of in vitro grown complex tissues) using hPSC-derived blood, bone, cartilage, and/or liver cells. In a manner similar to the BlueRock Therapeutics Agreement, we may pursue these additional RM and cellular therapy applications in collaboration with third-parties.

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Risk Factors

Our business is subject to substantial risk. Please carefully consider the section titled “Risk Factors” on page 5 of this prospectus for a discussion of the factors you should carefully consider before deciding to purchase the securities offered by this prospectus. These risks include, among others:

we are a development stage biopharmaceutical company with no current revenues or approved products, and limited experience developing new drug, biological and/or regenerative medicine candidates, which makes it difficult to assess our future viability;

we depend heavily on the success of AV-101, and we cannot be certain that we will be able to obtain regulatory approval for, or successfully commercialize, AV-101, or any product candidate;

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failures or delays in the commencement or completion of our planned clinical trials could delay, prevent or limit our ability to generate revenue and continue our business;

we face significant competition, and if we are unable to compete effectively, we may not be able to achieve or maintain significant market penetration or improve our results of operations;

some of our programs have been partially supported by government grants, which may not be available to us in the future;

if we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents that are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects; and

we have incurred significant net losses since inception and we will continue to incur substantial operating losses for the foreseeable future.

Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations. You should be able to bear a complete loss of your investment.

Corporate information

VistaGen Therapeutics, Inc., a Nevada corporation, is the parent of VistaGen Therapeutics, Inc. (dba VistaStem Therapeutics, Inc.), a wholly-owned California corporation founded in 1998. Our principal executive offices are located at 343 Allerton Avenue, South San Francisco, California 94080, and our telephone number is (650) 577-3600. Our website address is www.vistagen.com. The information contained on our website is not part of this prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website.

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RISK FACTORS

An investment in our securities involves a high degree of risk. You should consider the risks, uncertainties and assumptions described under Item 1A, "Risk Factors," in our Annual Report on Form 10-K for the fiscal year ended March 31, 2016, as well as subsequently filed Quarterly Reports on Form 10-Q, which risk factors are incorporated herein by reference, and may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future and any prospectus supplement related to a particular offering. The risks and uncertainties we have described in our Annual Report on Form 10-K for the fiscal year ended March 31, 2016 and subsequent Quarterly Reports on Form 10-Q are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations. The occurrence of any of these known or unknown risks might cause you to lose all or part of your investment in the offered securities.

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CAUTIONARY NOTES REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements contained in this prospectus and/or any applicable prospectus supplement other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important 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 the forward-looking statements.

The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “w,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

the availability of capital to satisfy our working capital requirements;

the accuracy of our estimates regarding expenses, future revenues and capital requirements;

our plans to develop and commercialize our lead product candidate, AV-101, initially as an adjunctive treatment for MDD in patients with an inadequate response to standard, FDA-approved antidepressants, and subsequently as a treatment for additional CNS diseases and disorders;

our ability to initiate and complete our clinical trials and to advance our product candidates into additional clinical trials, including pivotal clinical trials, and successfully complete such clinical trials;

regulatory developments in the U.S. and foreign countries;

the performance of the U.S. National Institute of Mental Health, our third-party contractors involved with the manufacturer and production of our drug candidates for nonclinical and clinical development activities, contract research organizations and other third-party nonclinical and clinical development collaborators and regulatory service providers;

our ability to obtain and maintain intellectual property protection for our core assets;

the size of the potential markets for our product candidates and our ability to serve those markets;

the rate and degree of market acceptance of our product candidates for any indication once approved;

the success of competing products and product candidates in development by others that are or become available for the indications that we are pursuing;

the loss of key scientific, clinical and nonclinical development, and/or management personnel, internally or from one of our third-party collaborators; and

other risks and uncertainties, including those described under Item 1A, "Risk Factors," in our Annual Report on Form 10-K for the fiscal year ended March 31, 2016 and subsequent Quarterly Reports on Form 10-Q, which risk factors are incorporated herein by reference.

These forward-looking statements are only predictions and we may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, so you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our business, financial condition and operating results. We have included important factors in the cautionary statements included in this prospectus, as well as certain information incorporated by reference into this prospectus, that could cause actual future results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements whether as a result of new information, future events or otherwise, except as required by applicable law.

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RATIO OF EARNINGS TO FIXED CHARGES

Our ratio of earnings to fixed charges for recently completed fiscal years and any required interim periods will be specified in a prospectus supplement or in a document that we file with the SEC and incorporated by reference in the future.

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USE OF PROCEEDS

Unless otherwise provided in the applicable prospectus supplement, we intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, including research and development, working capital and capital expenditures. We may use a portion of the net proceeds to fund production of, and nonclinical and clinical studies related to Phase 2 and Phase 3 development of, AV-101 and other drug candidates. We may also use the net proceeds from the sale of the securities under this prospectus to in-license, acquire or invest in complementary businesses, technologies, products or assets. However, we have no current commitments or obligations to do so. We may set forth additional information on the use of proceeds from the sale of the securities we offer under this prospectus in a prospectus supplement relating to the specific offering. We cannot currently allocate specific percentages of the net proceeds that we may use for the purposes specified above. As a result, our management will have broad discretion in the allocation of the net proceeds. Pending the application of the net proceeds, we intend to invest the net proceeds in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

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DESCRIPTION OF OUR CAPITAL STOCK

General

Our authorized capital stock consists of 30.0 million shares of common stock, \$0.001 par value per share, and 10.0 million shares of preferred stock, \$0.001 par value per share. The following is a description of our common stock and certain provisions of our Restated Articles of Incorporation (Articles), and our amended and restated bylaws (Bylaws), and certain provisions of Nevada law.

As of March 31, 2017, there were issued and outstanding, or reserved for issuance:

8,781,471 shares of common stock held by approximately 700 stockholders of record;

750,000 shares of common stock reserved for issuance upon conversion of 500,000 shares our Series A Preferred held by one institutional investor and one accredited individual investor;

1,160,240 shares of common stock reserved for issuance upon conversion of 1,160,240 shares of our Series B Preferred held by two institutional investors;

2,318,012 shares of common stock reserved for issuance upon conversion of 2,318,012 shares of our Series C Preferred held by one institutional investor;

4,549,006 shares of common stock that have been reserved for issuance upon exercise of outstanding warrants, with a weighted average exercise price of \$6.31 per share;

1,659,324 shares of common stock reserved for issuance upon exercise of outstanding stock options under our 1999 Stock Incentive Plan and our Amended and Restated 2016 Stock Incentive Plan, with a weighted average exercise price of \$4.76 per share; and

1,134,911 shares of common stock reserved for future issuance in connection with future grants under our Amended and Restated 2016 Stock Incentive Plan.

We may elect or be required to amend our Articles to increase the number of shares of common stock authorized for issuance prior to completing sales of shares of our common stock, or securities convertible and/or exchangeable into shares of our common stock described in this prospectus.

Common Stock

This section describes the general terms of our common stock that we may offer from time to time. For more detailed information, a holder of our common stock should refer to our Articles and our Bylaws, copies of which are filed with

the SEC as exhibits to the registration statement of which this prospectus is a part.

Except as otherwise expressly provided in our Articles, or as required by applicable law, all shares of our common stock have the same rights and privileges and rank equally, share ratably and are identical in all respects as to all matters, including, without limitation, those described below. All outstanding shares of common stock are fully paid and nonassessable.

Voting Rights

Each holder of our common stock is entitled to cast one vote for each share of common stock held on all matters submitted to a vote of stockholders. Cumulative voting for election of directors is not allowed under our Articles, which means that a plurality of the shares voted can elect all of the directors then outstanding for election. Except as otherwise provided under Nevada law or our Articles, and Bylaws, on matters other than election of directors, action on a matter is approved if the votes cast favoring the action exceed the votes cast opposing the action.

Dividend Rights

The holders of outstanding shares of our common stock are entitled to receive dividends out of funds legally available, if our board of directors, in its discretion, determines to issue dividend, and only at the times and in the amounts that our board of directors may determine. Our board of directors is not obligated to declare a dividend. We have not paid any dividends in the past and we do not intend to pay dividends in the foreseeable future.

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Liquidation Rights

Upon our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share equally, identically and ratably in all assets remaining, subject to the prior satisfaction of all outstanding debt and liabilities and the preferential rights and payment of liquidation preferences, if any, on any outstanding shares of preferred stock.

No Preemptive or Similar Rights

Our common stock is not subject to conversion, redemption, sinking fund or similar provisions.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A., Jersey City, New Jersey.

Preferred Stock

This section describes the general terms and provisions of our outstanding shares of preferred stock, as well as preferred stock that we may offer from time to time. The applicable prospectus supplement will describe the specific terms of the shares of preferred stock offered through that prospectus supplement, which may differ from the terms we describe below. We will file a copy of the certificate of designation that contains the terms of each new series of preferred stock with the SEC each time we issue a new series of preferred stock, and these certificates of designation will be incorporated by reference into the registration statement of which this prospectus is a part. Each certificate of designation will establish the number of shares included in a designated series and fix the designation, powers, privileges, preferences and rights of the shares of each series as well as any applicable qualifications, limitations or restrictions. A holder of our preferred stock should refer to the applicable certificate of designation, our Articles and the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) for more specific information.

We are authorized, subject to limitations prescribed by Nevada law, to issue up to 10.0 million shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each series and to fix the designation, powers, preferences and rights of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors can increase or decrease the number of shares of any series, but not below the number of shares of that series then outstanding, without any further vote or action by our stockholders. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in control of the Company and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock.

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Outstanding Series of Preferred Stock

Currently, there are three series of our preferred stock outstanding- Series A Convertible Preferred Stock, Series B 10% Convertible Preferred Stock, and Series C Convertible Preferred Stock. The rights and preferences associated with each series are summarized below.

Series A Preferred

General

In December 2011, our board of directors authorized the creation of a series of up to 500,000 shares of Series A Preferred. The Certificate of Designation of the Relative Rights and Preferences of the Series A Convertible Preferred Stock was filed with the Nevada Secretary of State effective December 20, 2011.

Conversion and Rank

At March 31, 2017, there were 500,000 shares of Series A Preferred outstanding, which shares are currently subject to beneficial ownership blockers and are exchangeable at the option of the holders into an aggregate of 750,000 shares of our common stock. The Series A Preferred ranks prior to our common stock for purposes of liquidation preference.

Conversion Restriction

At no time may a holder of shares of Series A Preferred convert shares of the Series A Preferred if the number of shares of common stock to be issued pursuant to such conversion would result in such holder beneficially owning (as determined in accordance with Section 13(d) of the Exchange Act and the rules thereunder) more than 9.99% of all of the common stock outstanding at such time; provided, however, that this limitation may be waived upon sixty-one (61) days' notice to us.

Dividend Rights

The Series A Preferred has no separate dividend rights. However, whenever the board of directors declares a dividend on the common stock, each holder of record of a share of Series A Preferred, or any fraction of a share of Series A Preferred, on the date set by the board of directors to determine the owners of the common stock of record entitled to receive such dividend (Record Date) shall be entitled to receive out of any assets at the time legally available therefor, an amount equal to such dividend declared on one share of common stock multiplied by the number of shares of common stock into which such share, or such fraction of a share, of Series A Preferred could be exchanged on the Record Date.

Voting Rights

The Series A Preferred has no voting rights, except with respect to transactions upon which the Series A Preferred shall be entitled to vote separately as a class, The common stock into which the Series A Preferred is exchangeable shall, upon issuance, have all of the same voting rights as other issued and outstanding shares of our common stock.

Liquidation Rights

In the event of the liquidation, dissolution or winding up of our affairs, after payment or provision for payment of our debts and other liabilities, the holders of Series A Preferred then outstanding shall be entitled to receive, out of our assets, if any, an amount per share of Series A Preferred calculated by taking the total amount available for distribution to holders of all of our outstanding common stock before deduction of any preference payments for the Series A Preferred, divided by the total of (x), all of the then outstanding shares of our common stock, plus (y) all of the shares of our common stock into which all of the outstanding shares of the Series A Preferred can be exchanged before any payment shall be made or any assets distributed to the holders of the common stock or any other junior stock.

Series B Preferred

General

In May 2015, our board of directors authorized the creation of a series of up to 4.0 million shares of Series B 10% Convertible Preferred Stock (Series B Preferred). The Certificate of Designation of the Relative Rights and Preferences of the Series B 10% Convertible Preferred Stock was filed with the Nevada Secretary of State on May 7, 2015 (the Series B Certificate of Designation).

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Conversion

Each share of Series B Preferred is convertible, at the option of the holder (Voluntary Conversion), into one (1) share of the Company's common stock. All outstanding shares of Series B Preferred are also automatically convertible into common stock (Automatic Conversion) upon the closing or effective date of any of the following transactions or events: (i) a strategic transaction involving AV-101 with an initial up front cash payment to the Company of at least \$10.0 million; (ii) a registered public offering of Common Stock with aggregate gross proceeds to the Company of at least \$10.0 million; or (iii) for 20 consecutive trading days the Company's Common Stock trades at least 20,000 shares per day with a daily closing price of at least \$12.00 per share; provided, however, that Automatic Conversion and Voluntary Conversion are subject to certain beneficial ownership blockers set forth in Section 6 of the Certificate of Designation.

Following the completion of our \$10.9 million underwritten public offering of our common stock in May 2016, which public offering occurred concurrently with and facilitated our listing on the Nasdaq Capital Market, approximately 2.4 million shares of Series B Preferred were converted automatically into approximately 2.4 million shares of our common stock pursuant to the Automatic Conversion provision. At March 31, 2017, there were 1,160,240 shares of Series B Preferred outstanding, which shares are currently subject to beneficial ownership blockers and are exchangeable at the option of the respective holders by Voluntary Conversion, or pursuant to Automatic Conversion to the extent not otherwise subject to beneficial ownership blockers, into an aggregate of 1,160,240 shares of our common stock.

Conversion Restriction

At no time may a holder of shares of Series B Preferred convert shares of the Series B Preferred, either by Voluntary Conversion or Automatic Conversion, if the number of shares of common stock to be issued pursuant to such conversion would result in such holder beneficially owning (as determined in accordance with Section 13(d) of the Exchange Act and the rules thereunder) more than 9.99% of all of the common stock outstanding at such time; provided, however, that this limitation may be waived upon sixty-one (61) days' notice to us.

Rank

The Series B Preferred ranks prior to our common stock, and pari passu with the Series A Preferred for purposes of liquidation preference.

Dividend Rights

Prior to either a Voluntary Conversion or Automatic Conversion, shares of Series B Preferred will accrue dividends, payable only in unregistered common stock, at a rate of 10% per annum (the Accrued Dividend). The Accrued Dividend will be payable on the date of either a Voluntary Conversion or Automatic Conversion solely in that number of shares of Common Stock equal to the Accrued Dividend.

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Voting Rights

The Series B Preferred has no voting rights, except with respect to transactions upon which the Series B Preferred shall be entitled to vote separately as a class. The common stock into which the Series B Preferred shall be exchangeable shall, upon issuance, have all of the same voting rights as other issued and outstanding shares of our common stock.

Liquidation Rights

Upon any liquidation, dissolution, or winding-up of the Company, whether voluntary or involuntary, the holders of Series B Preferred are entitled to receive out of the Company's assets, whether capital or surplus, an amount equal to the stated value of the Series B Preferred (\$7.00 per share), plus any accrued and unpaid dividends thereon, before any distribution or payment shall be made to the holders of any junior securities, including holders of our common stock. If the assets of the Company are insufficient to pay, in full, such amounts, then the entire assets to be distributed to the holders of the Series B Preferred shall be ratably distributed among the holders in accordance with the respective amounts that would be payable on such shares if all amounts payable thereon were paid in full.

Series C Preferred

General

In January 2016, our board of directors authorized the creation of a series of up to 3.0 million shares of Series C Convertible Preferred Stock (Series C Preferred). The Certificate of Designation of the Relative Rights and Preferences of the Series C Convertible Preferred Stock was filed with the Nevada Secretary of State, effective January 25, 2016 (the Series C Certificate of Designation).

Conversion and Rank

At March 31, 2017, there were 2,318,012 shares of Series C Preferred outstanding, which shares of Series C Preferred are currently subject to beneficial ownership blockers and are exchangeable at the option of the holder into 2,318,012 shares of our common stock. The Series C Preferred ranks prior to our common stock for purposes of liquidation preference, and pari passu with the Series A Preferred and Series B Preferred.

Conversion Restriction

At no time may a holder of shares of Series C Preferred convert shares of the Series C Preferred if the number of shares of common stock to be issued pursuant to such conversion would result in such holder beneficially owning (as determined in accordance with Section 13(d) of the Exchange Act and the rules thereunder) more than 9.99% of all of the common stock outstanding at such time; provided, however, that this limitation may be waived upon sixty-one (61) days' notice to us.

Dividend Rights

The Series C Preferred has no separate dividend rights. However, whenever the board of directors declares a dividend on the common stock, each holder of record of a share of Series C Preferred, or any fraction of a share of Series C Preferred, on the date set by the board of directors to determine the owners of the common stock of record entitled to receive such dividend (Record Date) shall be entitled to receive out of any assets at the time legally available therefor,

an amount equal to such dividend declared on one share of common stock multiplied by the number of shares of common stock into which such share, or such fraction of a share, of Series C Preferred could be exchanged on the Record Date.

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Voting Rights

The Series C Preferred has no voting rights, except with respect to transactions upon which the Series C Preferred shall be entitled to vote separately as a class. The common stock into which the Series C Preferred is exchangeable shall, upon issuance, have all of the same voting rights as other issued and outstanding shares of our common stock.

Liquidation Rights

In the event of the liquidation, dissolution or winding up of our affairs, after payment or provision for payment of our debts and other liabilities, the holders of Series C Preferred then outstanding shall be entitled to receive, out of our assets, if any, an amount per share of Series C Preferred calculated by taking the total amount available for distribution to holders of all of our outstanding common stock before deduction of any preference payments for the Series C Preferred, divided by the total of (x), all of the then outstanding shares of our common stock, plus (y) all of the shares of our common stock into which all of the outstanding shares of the Series C Preferred can be exchanged before any payment shall be made or any assets distributed to the holders of the common stock or any other junior stock.

Shares of Preferred Stock Issuable Pursuant to this Prospectus

We will incorporate by reference as an exhibit to the registration statement, which includes this prospectus, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. This description and the applicable prospectus supplement will include:

the title and stated value;

the number of shares authorized;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date, and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise such redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;

voting rights, if any, of the preferred stock;

preemptive rights, if any;

restrictions on transfer, sale or other assignment, if any;

a discussion of any material United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issue shares of preferred stock under this prospectus, the shares will fully be paid and nonassessable and will not have, or be subject to, any preemptive or similar rights.

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DESCRIPTION OF OUR WARRANTS

The following description, together with the additional information we include in any applicable prospectus supplements or free writing prospectus, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock and/or preferred stock in one or more series. Warrants may be offered independently or together with common stock and/or preferred stock offered by any prospectus supplement or free writing prospectus, and may be attached to or separate from those securities. While the terms we have summarized below will generally apply to any future warrants we may offer under this prospectus, we will describe the particular terms of any warrants that we may offer in more detail in the applicable prospectus supplement or free writing prospectus. The terms of any warrants we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below.

In the event that we issue warrants, we will issue the warrants under a warrant agreement which we will enter into with a warrant agent to be selected by us. Forms of these warrant agreements and forms of the warrant certificates representing the warrants, and the complete warrant agreements and forms of warrant certificates containing the terms of the warrants being offered, will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC. We use the term “warrant agreement” to refer to any of these warrant agreements. We use the term “warrant agent” to refer to the warrant agent under any of these warrant agreements. The warrant agent will act solely as an agent of ours in connection with the warrants and will not act as an agent for the holders or beneficial owners of the warrants.

The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement applicable to a particular series of warrants. We urge you to read the applicable prospectus supplements or free writing prospectus related to the warrants that we sell under this prospectus, as well as the complete warrant agreements that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement or free writing prospectus the terms relating to a series of warrants. If warrants for the purchase of common stock or preferred stock are offered, the prospectus supplement or free writing prospectus will describe the following terms, to the extent applicable:

the offering price and the aggregate number of warrants offered;

the total number of shares that can be purchased if a holder of the warrants exercises them and, in the case of warrants for preferred stock, the designation, total number and terms of the series of preferred stock that can be purchased upon exercise;

the designation and terms of any series of preferred stock with which the warrants are being offered and the number of warrants being offered with each share of common stock or preferred stock;

the date on and after which the holder of the warrants can transfer them separately from the related common stock or series of preferred stock;

the number of shares of common stock or preferred stock that can be purchased if a holder exercises the warrant and the price at which such common stock or preferred stock may be purchased upon exercise, including, if applicable, any provisions for changes to or adjustments in the exercise price and in the securities or other property receivable upon exercise;

the terms of any rights to redeem or call, or accelerate the expiration of, the warrants;

the date on which the right to exercise the warrants begins and the date on which that right expires;

federal income tax consequences of holding or exercising the warrants; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the warrants.

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Exercise of Warrants

Each holder of a warrant is entitled to purchase the number of shares of common stock or preferred stock, as the case may be, at the exercise price described in the applicable prospectus supplement or free writing prospectus. After the close of business on the day when the right to exercise terminates (or a later date if we extend the time for exercise), unexercised warrants will become void.

A holder of warrants may exercise them by following the general procedure outlined below:

delivering to the warrant agent the payment required by the applicable prospectus supplement or free writing prospectus to purchase the underlying security;

properly completing and signing the reverse side of the warrant certificate representing the warrants; and

delivering the warrant certificate representing the warrants to the warrant agent within five business days of the warrant agent receiving payment of the exercise price.

If you comply with the procedures described above, your warrants will be considered to have been exercised when the warrant agent receives payment of the exercise price, subject to the transfer books for the securities issuable upon exercise of the warrant not being closed on such date. After you have completed those procedures and subject to the foregoing, we will, as soon as practicable, issue and deliver to you the common stock or preferred stock that you purchased upon exercise. If you exercise fewer than all of the warrants represented by a warrant certificate, a new warrant certificate will be issued to you for the unexercised amount of warrants. Holders of warrants will be required to pay any tax or governmental charge that may be imposed in connection with transferring the underlying securities in connection with the exercise of the warrants.

Amendments and Supplements to the Warrant Agreements

We may amend or supplement a warrant agreement without the consent of the holders of the applicable warrants to cure ambiguities in the warrant agreement, to cure or correct a defective provision in the warrant agreement, or to provide for other matters under the warrant agreement that we and the warrant agent deem necessary or desirable, so long as, in each case, such amendments or supplements do not materially adversely affect the interests of the holders of the warrants.

Warrant Adjustments

Unless the applicable prospectus supplement or free writing prospectus states otherwise, the exercise price of, and the number of securities covered by, a common stock warrant or preferred stock warrant will be adjusted proportionately if we subdivide or combine our common stock or preferred stock, as applicable. In addition, unless the prospectus supplement or free writing prospectus states otherwise, if we, without receiving payment:

issue capital stock or other securities convertible into or exchangeable for common stock or preferred stock, or any rights to subscribe for, purchase or otherwise acquire any of the foregoing, as a dividend or distribution to holders of our common stock or preferred stock;

pay any cash to holders of our common stock or preferred stock other than a cash dividend paid out of our current or retained earnings or other than in accordance with the terms of the preferred stock;

issue any evidence of our indebtedness or rights to subscribe for or purchase our indebtedness to holders of our common stock or preferred stock; or

issue common stock or preferred stock or additional stock or other securities or property to holders of our common stock or preferred stock by way of spinoff, split-up, reclassification, combination of shares or similar corporate rearrangement,

then the holders of common stock warrants and preferred stock warrants, as applicable, will be entitled to receive upon exercise of the warrants, in addition to the securities otherwise receivable upon exercise of the warrants and without paying any additional consideration, the amount of stock and other securities and property such holders would have been entitled to receive had they held the common stock or preferred stock, as applicable, issuable under the warrants on the dates on which holders of those securities received or became entitled to receive such additional stock and other securities and property.

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Except as stated above or as otherwise set forth in the applicable prospectus supplement or free writing prospectus, the exercise price and number of securities covered by a common stock warrant and preferred stock warrant, and the amounts of other securities or property to be received, if any, upon exercise of those warrants, will not be adjusted or provided for if we issue those securities or any securities convertible into or exchangeable for those securities, or securities carrying the right to purchase those securities or securities convertible into or exchangeable for those securities.

Holders of common stock warrants and preferred stock warrants may have additional rights under the following circumstances:

certain reclassifications, capital reorganizations or changes of the common stock or preferred stock, as applicable;

certain share exchanges, mergers, or similar transactions involving us and which result in changes of the common stock or preferred stock, as applicable; or

certain sales or dispositions to another entity of all or substantially all of our property and assets.

If one of the above transactions occurs and holders of our common stock or preferred stock are entitled to receive stock, securities or other property with respect to or in exchange for their securities, the holders of the common stock warrants and preferred stock warrants then outstanding, as applicable, will be entitled to receive upon exercise of their warrants the kind and amount of shares of stock and other securities or property that they would have received upon the applicable transaction if they had exercised their warrants immediately before the transaction.

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DESCRIPTION OF OUR UNITS

This section outlines some of the provisions of the units and the unit agreements. This information may not be complete in all respects and is qualified entirely by reference to the unit agreement with respect to the units of any particular series. The specific terms of any series of units will be described in the applicable prospectus supplement or free writing prospectus. If so described in a particular prospectus supplement or free writing prospectus, the specific terms of any series of units may differ from the general description of terms presented below.

As specified in the applicable prospectus supplement, we may issue units consisting of one or more shares of common stock, shares of preferred stock, warrants or any combination of such securities.

The applicable prospectus supplement will specify the following terms of any units in respect of which this prospectus is being delivered:

the terms of the units and of any of the shares of common stock, shares of preferred stock or warrants comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately;

a description of the terms of any unit agreement governing the units;

if appropriate, a discussion of material U.S. federal income tax considerations; and

a description of the provisions for the payment, settlement, transfer or exchange of the units.

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DESCRIPTION OF CERTAIN PROVISIONS OF NEVADA LAW AND
OUR ARTICLES OF INCORPORATION AND BYLAWS

Transactions with Interested Persons

Under the Nevada Revised Statutes, or NRS, a transaction with the Company (i) in which a Company director or officer has a direct or indirect interest, or (ii) involving another corporation, firm or association in which one or more of the Company's directors or officers are directors or officers of the corporation, firm or association or have a financial interest in the corporation firm or association, is not void or voidable solely because of the director's or officer's interest or common role in the transaction if any one of the following circumstances exists:

the fact of the common directorship, office or financial interest is known to the board of directors or a committee of the board of directors and a majority of disinterested directors on the board of directors (or on the committee) authorized, approved or ratified the transaction;

the fact of the common directorship, office or financial interest is known to the stockholders and disinterested stockholders holding a majority of the shares held by disinterested stockholders authorized, approved or ratified the transaction;

the fact of the common directorship, office or financial interest is not known to the director or officer at the time the transaction is brought to the board of directors for action; or

the transaction was fair to the Company at the time it is authorized or approved.

Control Share Acquisition Provisions

Nevada law precludes an acquirer of the shares of a Nevada corporation who crosses one of three ownership thresholds (20%, 33 1/3% or 50%) from obtaining voting rights with respect to those shares unless the disinterested holders of a majority of the shares of the Company held by disinterested stockholders vote to accord voting power to those shares.

Combinations with Interested Stockholders

Under the NRS, except under certain circumstances, a corporation is not permitted to engage in a business combination with any "interested stockholder" for a period of two years following the date such stockholder became an interested stockholder. An "interested stockholder" is a person or entity who owns 10% or more of the outstanding shares of voting stock. Nevada permits a corporation to opt out of the application of these business combination provisions by so providing in the articles of incorporation or bylaws. The Company's Bylaws contain a provision opting out of the application of these business combination provisions.

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PLAN OF DISTRIBUTION

We may sell the securities described in this prospectus to or through underwriters or dealers, through agents, or directly to one or more purchasers. A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

the name or names of any underwriters or agents, if applicable;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in a prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement that names the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act of 1933, as amended (the Securities Act), or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the NASDAQ Capital Market may engage in passive market making transactions in accordance with Rule 103 of Regulation M during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded.

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LEGAL MATTERS

The validity of the securities offered by this prospectus will be passed upon by Disclosure Law Group, a Professional Corporation, San Diego, California (DLG). Partners of DLG beneficially own an aggregate of 65,987 registered and/or restricted shares of our common stock.

EXPERTS

The financial statements of the Company incorporated in this prospectus by reference to the Annual Report on Form 10-K for the fiscal year ended March 31, 2016 have been audited by OUM & Co. LLP, an independent registered public accounting firm, as set forth in their report thereon.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference room at 100 F Street, NE, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available, at no charge, to the public at the SEC's website at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The following documents filed by us with the SEC are incorporated by reference in this prospectus:

Annual Report on Form 10-K for the fiscal year ended March 31, 2016, filed on June 24, 2016;

Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, filed on August 12, 2016;

Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, filed on November 14, 2016;

Quarterly Report on Form 10-Q for the quarter ended December 31, 2016, filed on February 13, 2017;

Current Report on Form 8-K filed on May 16, 2016;

Current Report on Form 8-K filed on June 22, 2016;

Current Report on Form 8-K filed on August 17, 2016;

Current Report on Form 8-K filed on September 27, 2016;

Current Report on Form 8-K filed on December 14, 2016;

Current Report on Form 8-K filed on March 29, 2017; and

The description of our common stock contained in the Registration Statement on Form 8-A filed pursuant to Section 12(b) of the Exchange Act on May 3, 2016, including any amendment or report filed with the SEC for the purpose of

updating this description.

We also incorporate by reference all documents we file pursuant to Section 13(a), 13(c), 14 or 15 of the Exchange Act (other than any portions of filings that are furnished rather than filed pursuant to Items 2.02 and 7.01 of a Current Report on Form 8-K) after the date of the initial registration statement of which this prospectus is a part and prior to effectiveness of such registration statement. All documents we file in the future pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the termination of the offering are also incorporated by reference and are an important part of this prospectus.

Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for the purposes of this registration statement to the extent that a statement contained herein or in any other subsequently filed document which also is or deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this registration statement.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, a copy of any or all of the information that has been incorporated by reference in the prospectus but not delivered with the prospectus. You may request a copy of these filings, excluding the exhibits to such filings which we have not specifically incorporated by reference in such filings, at no cost, by writing to or calling us at:

VistaGen Therapeutics, Inc.
Attn: Corporate Secretary
343 Allerton Avenue
South San Francisco, CA 94080
(650) 577-3600

This prospectus is part of a registration statement we filed with the SEC. You should only rely on the information or representations contained in this prospectus and any accompanying prospectus supplement. We have not authorized anyone to provide information other than that provided in this prospectus and any accompanying prospectus supplement. We are not making an offer of the securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or any accompanying prospectus supplement is accurate as of any date other than the date on the front of the document.

1,371,430 Shares

Series A1 Warrants to Purchase up to 1,338,931 Shares of Common Stock

Series A2 Warrants to Purchase up to 503,641 Shares of Common Stock

Prospectus Supplement

Oppenheimer & Co.

August 31, 2017