As submitted confidentially with the Securities and Exchange Commission on March 27, 2017. This draft registration statement has not been publicly filed with the Securities and Exchange Commission and all information herein remains strictly confidential.

Registration No. 333-

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-1
REGISTRATION STATEMENT

UNDER
THE SECURITIES ACT OF 1933

Avenue Therapeutics, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**2834**	**47-4113275**
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification Number)

2 Gansevoort Street, 9th Floor
New York, New York 10014
(781) 652-4500

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Lucy Lu, M.D.
Interim President & CEO
2 Gansevoort Street, 9th Floor
New York, New York 10014
(781) 652-4500

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent For Service)

Copies to:

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New York, NY 10016	**New York, NY 10017**
(212) 210-9400	**(212) 935-3000**

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☐
Non-accelerated filer ☒ (Do not check if a smaller reporting company)	Smaller reporting company ☐

CALCULATION OF REGISTRATION FEE

Title Of Each Class Of Securities To Be Registered	Proposed Maximum Aggregate Offering Price (1)	Amount Of Registration Fee (2)
Common Stock, par value $0.0001 per share	$	$

(1) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457 under the Securities Act of 1933.

(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

TABLE OF CONTENTS

The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 27, 2017

PRELIMINARY PROSPECTUS

shares

Common Stock

This is the initial public offering of our common stock. No public market currently exists for our common stock. We are offering all of the shares of common stock offered by this prospectus. We expect the public offering price to be between $ and $ per share.

We have applied to list our common stock on the NASDAQ Capital Market under the symbol "ATXI." No assurance can be given that our application will be approved.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act and may elect to comply with certain reduced reporting requirements. See the section titled "Implications of Being an Emerging Growth Company."

Investing in our common stock involves risks. See "Risk Factors" beginning on page 9.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions (1)	$	$
Proceeds to Avenue, before expenses	$	$

(1) See "Underwriting" for additional disclosure regarding underwriting discounts, commissions and expenses.

The underwriters may also purchase up to an additional shares of our common stock at the public offering price, less the underwriting discounts and commissions payable by us, to cover over-allotments, if any, within 30 days from the date of this prospectus. If the underwriters exercise this option in full, the total underwriting discounts and commissions will be $ and our total proceeds, after deducting underwriting discounts and commissions but before expenses, will be $.

The underwriters are offering the common stock as set forth under "Underwriting." The underwriters expect to deliver the shares on or about , 2017.

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

Sole Book-Running Manager

RAYMOND JAMES

Co-Manager

NATIONAL SECURITIES CORPORATION

The date of this prospectus is , 2017.

TABLE OF CONTENTS

Neither we nor the underwriters have authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where such offers and sales are permitted. The information in this prospectus is accurate only as of its date, regardless of its time of delivery or of any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

ABOUT THIS PROSPECTUS

In this prospectus, unless the context suggests otherwise, references to "Avenue Therapeutics," "Avenue," the "Company," "we," "us" and "our" refer to Avenue Therapeutics, Inc.

This prospectus describes the specific details regarding this offering and the terms and conditions of the common stock being offered hereby and the risks of investing in our common stock. You should read this prospectus, any free writing prospectus and the additional information about us described in the section entitled "*Where You Can Find More Information*" before making your investment decision.

Neither we, nor any of our officers, directors, agents or representatives or underwriters, make any representation to you about the legality of an investment in our common stock. You should not interpret the contents of this prospectus or any free writing prospectus to be legal, business, investment or tax advice. You should consult with your own advisors for that type of advice and consult with them about the legal, tax, business, financial and other issues that you should consider before investing in our common stock.

INDUSTRY AND MARKET DATA

This prospectus includes industry and market data that we obtained from periodic industry publications, third party studies and surveys, filings of public companies in our industry and internal company surveys. These sources include government and industry sources. Industry publications and surveys generally state that the information contained therein has been obtained from sources believed to be reliable. Although we believe the industry and market data to be reliable as of the date of this prospectus, this information could prove to be inaccurate. Industry and market data could be wrong because of the method by which sources obtained their data and because information cannot always be verified with complete certainty due to the limits on the availability and reliability of raw data, the voluntary nature of the data gathering process and other limitations and uncertainties. In addition, we do not know all of the assumptions regarding general economic conditions or growth that were used in preparing the forecasts from the sources relied upon or cited herein.

IMPLICATIONS OF BEING AN EMERGING GROWTH COMPANY

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, and may take advantage of certain exemptions from reporting requirements that are otherwise applicable to public companies. We may take advantage of these provisions until the earlier of (i) the last day of our fiscal year following the fifth anniversary of the closing of this offering, (ii) the last day of the fiscal year (a) in which we have total annual gross revenue of at least $1.0 billion or (b) in which we are deemed to be a large accelerated filer, which means the market value of our equity securities that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter, and (iii) the date on which we have issued more than $1.0 billion of non-convertible debt in any three-year period. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and being exempt from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. Additionally, as an emerging growth company, we have elected to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. As such, our financial statements may not be comparable to companies that comply with public company effective dates. We cannot predict if investors will find our shares less attractive because we may rely on these provisions. If some investors find our shares less attractive as a result, there may be a less active trading market for our shares and our share price may be more volatile.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary may not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus carefully, including the "Risk Factors" section and the financial statements and the notes thereto contained elsewhere in this prospectus before deciding to invest in our common stock.

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of an intravenous, or IV, formulation of tramadol HCl, or IV Tramadol, for the management of moderate to moderately severe postoperative pain. Tramadol is a synthetic dual-acting opioid with a well-established efficacy and safety profile, and has been used throughout the world for more than 30 years, accumulating an abundance of available clinical data. Oral tramadol is currently approved and marketed in the United States for moderate to moderately severe pain in adults, and physicians are already familiar with the oral dosage of the drug. Parenteral tramadol is approved and used for the management of moderate to moderately severe postoperative pain throughout much of the world, but there is no parenteral formulation currently available in the United States. We anticipate that the introduction of an intravenous formulation in the United States will address the current market need for an intravenous dosage of tramadol, in addition to many of the shortcomings of opioids and other analgesics currently used in the postoperative setting. We have an exclusive license to develop and commercialize IV Tramadol in the United States. We also plan to seek additional products and to develop them in the acute/intensive care hospital market.

In 2016, we completed a pharmacokinetics, or PK, study for IV Tramadol in healthy volunteers as well as an End-of-Phase 2, or EOP2, meeting with the U.S. Food and Drug Administration, or the FDA. We plan to initiate a Phase 3 development program of IV Tramadol for the management of postoperative pain in 2017. We intend to conduct two pivotal Phase 3 trials for IV Tramadol. We plan to initiate the first Phase 3 trial in patients with moderate-to-severe pain following bunionectomy in the third quarter of 2017. We anticipate that we will have topline data as early as the second quarter of 2018. We plan to initiate the second Phase 3 trial in patients with moderate-to-severe pain following abdominoplasty in the third quarter of 2018, upon successful completion of the bunionectomy study. Based on the enrollment pace of similar studies, we anticipate that we will have topline data from this second Phase 3 trial as early as mid-2019. We also plan to conduct an open-label safety study, which will run concurrently with the two Phase 3 trials. If these studies are successful, we plan to submit a new drug application, or an NDA, for IV Tramadol to treat moderate to moderately severe postoperative pain pursuant to Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or FDCA, by the end of 2019.

Our Strategy

Our primary objective is to establish IV Tramadol as an invaluable part of a treating physician's repertoire of available pharmaceutical options for the management of postoperative pain. The key elements of our strategy include:

- *Complete our Phase 3 program for IV Tramadol.* We expect to commence our Phase 3 program in the third quarter of 2017 and expect to report topline data from our two pivotal trials as early as the second quarter of 2018 and mid-2019, respectively. We also plan to conduct an open-label safety study, which will run concurrently with the two Phase 3 trials.
- *Obtain FDA approval of IV Tramadol for the management of moderate to moderately severe postoperative pain.* If our Phase 3 trials meet their primary endpoints, we plan to submit our NDA for IV Tramadol by the end of 2019. We intend to seek FDA approval of IV Tramadol pursuant to Section 505(b)(2) of the FDCA.

- *Commercially launch IV Tramadol in the United States.* We intend to directly commercialize IV Tramadol in the United States, if approved, using a small hospital-based sales force. Alternatively, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidate.
- *Maintain, expand and protect our intellectual property portfolio.* We intend to expand and protect our intellectual property in the area of IV administration of tramadol in order to maintain a defensible and valuable intellectual property portfolio.
- *Expand our product portfolio through acquiring or in-licensing additional late-stage, or new versions of currently approved hospital-focused products.* We will seek additional opportunities to acquire or in-license products to more fully utilize our clinical, regulatory, manufacturing, sales and marketing capabilities. To reduce the time-to-market and the risks and costs of clinical development, we are focusing on products that are in late-stages of development, currently commercialized outside the United States or approved in the United States but with significant commercial potential for proprietary new uses or formulations.
- *Pursue additional indications and commercial opportunities for our product candidates.* We will seek to maximize the value of IV Tramadol and any other product candidates we may in-license, acquire or develop by pursuing other indications and commercial opportunities for such candidates.

Competition

Competition in the pharmaceutical and biotechnology industries is intense. Our competitors include pharmaceutical companies and biotechnology companies, as well as universities and public and private research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. To compete successfully in this industry we must identify novel and unique drugs or methods of treatment and then complete the development of those drugs as treatments in advance of our competitors.

We believe that IV Tramadol will compete with a number of opioid and non-opioid drugs that are currently available for the management of acute pain or in development. The most commonly used opioids in the postoperative and acute pain settings are morphine, hydromorphone and fentanyl. The non-opioid drugs used in this setting include Ofirmev (IV acetaminophen) and IV formulations of nonsteroidal anti-inflammatory drugs, or NSAIDS, such as Dyloject (diclofenac), Toradol (ketorolac), and Caldolor (ibuprofen). In addition, we also expect to compete with agents such as Exparel, a liposome injection of bupivacaine indicated for administration into the surgical site to produce postsurgical analgesia.

In addition to approved products, there are a number of product candidates in development for the management of acute pain. The late-stage pain development pipeline is replete with reformulations and fixed-dose combination products of already available therapies. Among specific drug classes, opioid analgesics and NSAIDs represent the greatest number of agents in development. Most investigational opioids that have reached the later stages of clinical development are new formulations of already marketed opioids. Likewise, investigational NSAIDs — mostly lower dose injectable reformulations of already approved compounds — are another significant area of late-stage drug development in the postoperative pain space. There are also several agents with novel mechanisms in clinical development, such as CR845 (Cara Therapeutics, Inc.) and TRV130 (Trevena, Inc.).

U.S. Postoperative Pain Market Overview

We were formed to develop and market pharmaceutical products for the acute care setting in the United States. Our initial focus will be on developing our proprietary product candidate, IV Tramadol, for moderate to moderately severe postoperative pain. Even though the postoperative pain market is entrenched with low cost, generic pain relievers, we believe that there still remains a significant unmet medical need for safer and better-tolerated painkillers, which are also referred to as analgesics.

According to Decision Resources' Acute Pain Report of October 2014, or the 2014 Pain Report, sales of analgesics delivered via parenteral routes (IV, subcutaneous, and intramuscular injections) for the management of acute pain totaled approximately $965 million in the United States in 2013. According to the 2014 Pain Report, there were approximately 9 million select common inpatient procedures performed, all of which likely required postoperative pain management, in the United States in 2013. According to IMS Health, injectable analgesics sold approximately $1 billion in the United States in 2015.

The major goal in the management of postoperative pain is minimizing the dose of medications to lessen side effects while still providing adequate analgesia/pain relief. This is best accomplished with multimodal and preemptive analgesia. An effective pain relief program should be individualized for the particular patient, operation, and circumstances. In clinical practice, as there is no standard set of guidelines to treat postoperative pain, hospitals and even hospital units have their own practice guidelines that are often well entrenched in physicians' prescribing practices. These local guidelines are rooted in physician experience as it relates to anticipated severity of pain due to a particular surgical procedure, and are often modified with consideration to things like staffing limitations, availability of specific drugs and/or formulations, access to patient controlled analgesia, or PCA, systems, and formulary restrictions. Thus, treatment regimens vary widely from hospital to hospital, physician to physician and patient to patient.

Understanding the range of available interventions and considering the type of surgery is essential to safe and effective pain management. The general consensus among pain management practitioners is that use of more than one modality (i.e., molecules with different mechanisms or with different routes of administration) is optimal for successful postoperative pain management. The most commonly prescribed agents in the immediate postoperative pain market are typically acetaminophen, or APAP, NSAIDS, and opioid analgesics. APAP and NSAIDs are not sufficiently effective as the sole agent for pain management after major surgery in most patients. However, when used in conjunction with opioids, APAP and NSAIDs offer substantial benefits as the quality of analgesia is often improved or enhanced due to their differentiated mechanism of action. Nevertheless, the substantial side effects associated with these agents represent an important concern for patients and physicians to address. NSAIDS in particular have their own serious side effects, including increased post-surgery bleeding, peptic ulcer disease and renal impairment, and is associated with hepatic side effects.

We believe that, if approved, IV Tramadol will be an attractive option for physicians who treat postoperative pain. Tramadol is an established analgesic that physicians are already familiar with, and has documented efficacy and safety for moderate to moderately severe pain. In addition, as a Schedule IV controlled substance, tramadol has less potential for addiction and abuse than other narcotics widely prescribed for the management of postoperative pain. Combined with the availability of step-down therapy, we believe IV Tramadol's differentiated safety profile could make it an attractive alternative in the management of acute postoperative pain.

Risks to Consider

Before investing in our common stock, you should carefully consider all the information in this prospectus, including matters set forth under the heading "Risk Factors." We are a "controlled company" within the meaning of the NASDAQ listing standards and, as a result, qualify for, and rely on, exemptions from certain corporate governance requirements. You will not have the same protections afforded to stockholders of companies that are subject to such requirements.

Corporate Information

We were incorporated in Delaware on February 9, 2015. Our executive offices are located at 2 Gansevoort St., 9th Floor, New York, NY 10014. Our telephone number is 781-652-4500, and our website is *www.avenuetx.com*. We are a Delaware corporation, which is majority-owned and controlled by Fortress. Fortress is a biopharmaceutical company focused on acquiring, developing and commercializing novel pharmaceutical and biotechnology products and was incorporated in Delaware in June 2006. Following the completion of this offering, Fortress will maintain voting control of us. See "Relationships and Related Transactions" for a description of our relationship with Fortress. In addition, in September 2016, Fortress acquired 56.1% of National Holdings, Inc., which owns National Securities Corp., which is a FINRA member and will participate in this offering. See "Relationships and Related Transactions" and "Underwriting" for additional information.

THE OFFERING

Common stock offered by us	shares
Common stock outstanding before this offering	10,024,405 shares
Underwriters' option to purchase additional shares	shares
Common stock to be outstanding after this offering	shares (or shares if the underwriters exercise in full their option to purchase additional shares).
Use of Proceeds	We expect to use the net proceeds from this offering as follows: • approximately $30 million to fund our continued clinical research and development initiatives in connection with IV Tramadol; • approximately $6 million to pay off our debts to Fortress and NSC; and • the remainder, if any, to fund general corporate initiatives, including preliminary commercial preparation, and for general corporate purposes. See "Use of Proceeds" beginning on page 42 of this prospectus for more information.
Risks Factors	See "Risk Factors" beginning on page 9 in addition to other information in this prospectus for a discussion of factors you should consider carefully before deciding to invest in shares of our common stock.
Proposed NASDAQ symbol	We have applied to list our common stock on the NASDAQ Capital Market under the symbol "ATXI." No assurance can be given that our application will be approved.

The number of shares of our common stock to be outstanding after this offering is based on 10,023,810 shares of our common stock outstanding as of December 31, 2016, representing 9,773,810 shares of our common stock outstanding and 250,595 shares of our common stock issued to Fortress pursuant to the PIK Dividend, and excludes the following:

- 2,000,000 shares of our common stock reserved for issuance under our 2015 Incentive Plan (there have been no options granted or other securities issued under our 2015 Incentive Plan);
- shares of our common stock convertible upon the completion of our initial public offering related to the sale of convertible notes in December 2016 in the aggregate amount of $200,000; and
- shares underlying a warrant to be issued to National Securities Corporation following our initial public offering.

Unless otherwise indicated, all information in this prospectus reflects and assumes no exercise of the underwriters' option to purchase an additional shares of our common stock.

SUMMARY FINANCIAL AND OTHER DATA

The following tables summarize our financial data and should be read together with the section in this prospectus entitled "Management's Discussion and Analysis of Financial Condition and results of operations" and our financial statements and related notes included elsewhere in this prospectus. Our financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America, or GAAP. We have no subsidiaries.

The following tables summarize our financial data. We have derived the following statements of operations data for the year ended December 31, 2016 and for the period from February 9, 2015 (inception) to December 31, 2015 from our audited financial statements. We have also derived the balance sheet data for the years ended December 31, 2016 and December 31, 2015 from our audited financial statements. Our historical results are not necessarily indicative of the results that should be expected in the future.

(in thousands, except per share amounts)	For The Year Ended December 31, 2016	For The Period from February 9, 2015 (Inception) through December 31, 2015
Operating expenses:		
Research and development	$ 1,331	$ 961
Research and development – licenses acquired	49	3,040
General and administration	997	842
Loss from operations	(2,377)	(4,843)
Interest expense	420	215
Interest expense – related party	192	168
Change in fair value of warrant liabilities	188	—
Net Loss	**$ (3,177)**	**$ (5,226)**
Net loss per common share outstanding, basic and diluted	$ (0.37)	$ (0.64)
Weighted average number of common shares outstanding, basic and diluted	8,581,578	8,107,209

	December 31, 2016	December 31, 2015	Pro Forma	Pro Forma as Adjusted (1)
ASSETS				
Current Assets:				
Cash	$ 197	$ 14	$	$
Total Assets	**$ 197**	**$ 14**	$	$
LIABILITIES AND STOCKHOLDERS' DEFICIT				
Current Liabilities:				
Accounts payable and accrued expenses	$ 506	$ 491		
Accrued expenses – related party	1,348	511		
Interest payable	57	—		
Accrued interest – related party	346	165		
Notes payable – related party	2,848	1,165		
NSC notes payable, short-term	1,000	—		
Derivative warrant liability	314	114		
Total current liabilities	6,419	2,446		
Convertible notes payable, at fair value	200	—		
NSC notes payable, long-term (net of debt discount of $174 and $297, respectively)	1,826	2,703		
Total Liabilities	8,445	5,149		
Commitments and Contingencies				
Stockholders' Deficit				
Preferred Stock ($0.0001 par value), 2,000,000 shares authorized				
Class A Preferred Stock, 250,000 and 0 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—	—		
Common Stock ($0.0001 par value), 50,000,000 shares authorized				
Class A Common Stock, 0 and 7,000,000 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—	1		
Common shares; 9,773,810 and 2,150,000 shares issued and outstanding as of December 31, 2016 and 2015, respectively	1	—		
Common stock issuable, 250,595 and 228,750 shares as of December 31, 2016 and 2015, respectively	49	40		
Additional paid-in capital	105	50		
Accumulated deficit	(8,403)	(5,226)		
Total Stockholders' Deficit	(8,248)	(5,135)		
Total Liabilities and Stockholders' Deficit	**$ 197**	**$ 14**	$	$

(1) The December 31, 2016 as adjusted balance sheet data reflects the sale of shares of our common stock in this offering, assuming an initial public offering price of $ per share (the mid-point of the price range set forth on the cover page of this prospectus), after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase (decrease) each of cash and cash equivalents, additional paid-in capital, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions.

An increase (decrease) of one million shares in the number of shares offered by us in the assumed initial public offering would increase our net tangible book value after this offering by approximately $ million, or $ per share, and decrease the dilution per share to new investors by approximately $ per share, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The number of shares of our common stock to be outstanding after this offering is based on 10,023,810 shares of our common stock outstanding as of December 31, 2016, and excludes the following:

- 2,000,000 shares of our common stock reserved for issuance under our 2015 Incentive Plan (there have been no options granted or other securities issued under our 2015 Incentive Plan);
- shares of our common stock convertible upon the completion of our initial public offering related to the sale of convertible notes in December 2016 in the aggregate amount of $200,000; and
- shares underlying a warrant to be issued to National Securities Corporation following our initial public offering.

RISK FACTORS

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in the forward-looking statements we have made in this prospectus and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this prospectus and any related free writing prospectus, before making an investment decision. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Risks Related to Our Business and Industry

We currently have no drug products for sale, and only one drug product candidate, IV Tramadol. We are dependent on the success of IV Tramadol and cannot guarantee that we will be able to complete the required studies or that this product candidate will receive regulatory approval or be successfully commercialized.

Our business success depends ultimately on our ability to obtain regulatory approval for and successfully commercialize our only product candidate, IV Tramadol, and any significant delays in obtaining approval for and commercializing IV Tramadol will have a substantial adverse impact on our business and financial condition.

If approved, our ability to generate revenues from IV Tramadol will depend on our ability to:

- hire, train, deploy and support our sales force;
- create market demand for IV Tramadol through our own marketing and sales activities, and any other arrangements to promote this product candidate we may later establish;
- obtain sufficient quantities of IV Tramadol from our third party manufacturers as required to meet commercial demand at launch and thereafter;
- establish and maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- obtain and maintain government and private payer reimbursement for our product; and
- maintain patent protection and regulatory exclusivity for IV Tramadol.

We may not receive regulatory approval for IV Tramadol or future product candidates, or its or their approvals may be delayed, which would have a material adverse effect on our business and financial condition.

IV Tramadol and other future product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the European Medicines Agency, or the EMA, and similar regulatory authorities outside the United States. Failure to obtain marketing approval for our product candidate IV Tramadol or any future product candidates will prevent us from commercializing the product candidates. We have not received approval to market IV Tramadol from regulatory authorities in any jurisdiction. We have only limited experience in conducting preclinical and clinical studies and filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party contract research organizations as well as consultants and vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities.

Our product candidate IV Tramadol or any future product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If our product candidate or any future product candidate receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product. In addition, our third party supplier may not pass an inspection by the FDA of its manufacturing facilities and we may be forced to identify, qualify and implement additional suppliers.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if approval is granted at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical studies or clinical trials. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidate or any future product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenue will be materially impaired.

In addition, even if we were to obtain approval, regulatory authorities may approve our product candidate or any future product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our product, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of these scenarios could compromise the commercial prospects for our product candidate or any future product candidates.

If IV Tramadol is approved and our contract manufacturer fails to produce the product in the volumes that we require on a timely basis, to produce the product according to the applicable quality standards and requirements, or to comply with stringent regulations applicable to pharmaceutical drug manufacturers, we may face delays in the commercialization of this product candidate, lose potential revenues or be unable to meet market demand.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls, and the use of specialized processing equipment. We have entered into a development and supply agreement for the completion of pre-commercialization manufacturing development activities and the manufacture of commercial supplies of IV Tramadol. Any termination or disruption of this relationship may materially harm our business and financial condition, and frustrate any commercialization efforts for this product candidate.

In order to meet anticipated demand for IV Tramadol, if this product candidate is approved, we have one manufacturer to provide us clinical and commercial supply of IV Tramadol in accordance with the Current Good Manufacturing Practice, or cGMP. We also plan to qualify a backup manufacturer.

All of our contract manufacturers must comply with strictly enforced federal, state and foreign regulations, including cGMP requirements enforced by the FDA through its facilities inspection program, as well as controlled substance handling and security requirements, and we have little control over their compliance with these regulations. Any failure to comply with applicable regulations may result in fines and civil penalties, suspension of production, suspension or delay

in product approval, product seizure or recall, or withdrawal of product approval, and would limit the availability of our product. Any manufacturing defect or error discovered after products have been produced and distributed could result in even more significant consequences, including costly recall procedures, re-stocking costs, damage to our reputation and potential for product liability claims.

If the commercial manufacturers upon whom we rely to manufacture IV Tramadol, and any other product candidates we may in-license, fail to deliver the required commercial quantities on a timely basis at commercially reasonable prices, we would likely be unable to meet demand for our products and we would lose potential revenues.

If serious adverse or unacceptable side effects are identified during the development of IV Tramadol or our future product candidates, we may need to abandon or limit our development of some of our product candidates.

If our product candidate or future product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In our industry, many compounds that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the compound. In the event that our preclinical or clinical trials reveal a high and unacceptable severity and prevalence of side effects, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development or deny approval of our product candidate or future product candidates for any or all targeted indications. The FDA could also issue a letter requesting additional data or information prior to making a final decision regarding whether or not to approve a product candidate. The number of requests for additional data or information issued by the FDA in recent years has increased, and resulted in substantial delays in the approval of several new drugs. Undesirable side effects caused by our product candidate or future product candidates could also result in the inclusion of serious risk information in our product labeling, application of burdensome post-market requirements, or denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing and generating revenues from the sale of our product candidate. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial and could result in potential product liability claims.

For example, some of the adverse events observed in the IV Tramadol clinical trials completed to date include nausea, dizziness, drowsiness, tiredness, sweating, vomiting, dry mouth, somnolence and hypotension.

Additionally, if one or more of our current or future product candidates receives marketing approval, and we or others later identify undesirable side effects caused by this product, a number of potentially significant negative consequences could result, including:

- regulatory authorities may require the addition of serious risk-related labeling statements, specific warnings, precautions, or contraindication;
- regulatory authorities may suspend or withdraw their approval of the product, or require it to be removed from the market;
- regulatory authorities may require implementation of burdensome post-market risk mitigation strategies and practices;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product; or
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining marketing approval and market acceptance of our product candidate or future product candidates or could substantially

increase our commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenues from its sale.

Even if IV Tramadol receives regulatory approval, it and any other products we may market will remain subject to substantial regulatory scrutiny.

IV Tramadol and any other product candidates we may license or acquire will also be subject to ongoing requirements and review of the FDA and other regulatory authorities. These requirements include, among others, labeling, packaging, storage, advertising, promotion, record-keeping and submission of safety and other post-market information and reports, registration and listing requirements, ongoing cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping of the drug.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and off-label information and if we do not market our products for only their approved indications and on-label information, we may be subject to enforcement action for off-label marketing as well as false claims liability. Violations of the FDCA relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, operations, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits;
- suspension or withdrawal of marketing or regulatory approvals;
- suspension of any ongoing clinical trials;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

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

We will need to obtain FDA approval of any proposed product brand names, and any failure or delay associated with such approval may adversely impact our business.

A pharmaceutical product candidate cannot be marketed in the United States or other countries until we have completed a rigorous and extensive regulatory review processes, including approval of a brand name. Any brand names we intend to use for our product candidates will require approval from the FDA regardless of whether we have secured a formal trademark registration from the U.S. Patent and Trademark Office, or USPTO. The FDA typically conducts a review of proposed product brand names, including an evaluation of potential for confusion with other product names. The FDA may also object to a product brand name if it believes the name inappropriately implies medical claims. If the FDA objects to any of our proposed product brand names, we may be required to adopt an alternative brand name for our product candidates. If we adopt an alternative brand name, we would lose the benefit of our existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product brand name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. We may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit our ability to commercialize our product candidates.

Our current and future relationships with customers and third party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third party payors, distributors, retailers, marketers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and similar state or foreign laws which may constrain the business or financial arrangements and relationships through which we sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to transparency laws and patient privacy regulation by U.S. federal and state governments and by governments in foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include, but are not necessarily limited to:

- the federal Anti-Kickback Statute, which 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, or in return for, 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 and state healthcare programs, such as Medicare and Medicaid;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which impose criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent, making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, or the knowing retention of an overpayment from government health care programs; the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose obligations on covered healthcare providers, health plans, and healthcare clearinghouses, as well as their business associates that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Open Payments program, which requires manufacturers of certain drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to "payments or other transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and certain teaching hospitals and applicable manufacturers to report annually to CMS ownership and investment interests held by the physicians and their immediate family members. Data collection began on August 1, 2013 with requirements for manufacturers to submit reports to CMS by March 31, 2014 and 90 days after the end of each subsequent calendar year. Disclosure of such information was made by CMS on a publicly available website beginning in September 2014; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including our collaborators, is found not to be in compliance with applicable laws, it may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

Regulatory approval for any approved product is limited by the FDA to those specific indications and conditions for which clinical safety and efficacy have been demonstrated.

Any regulatory approval is limited to those specific diseases and indications for which a product is deemed to be safe and effective by the FDA. In addition to the FDA approval required for new formulations, any new indication for an approved product also requires FDA approval. If

we are not able to obtain FDA approval for any desired future indications for our products, our ability to effectively market and sell our products may be reduced and our business may be adversely affected.

While physicians may choose to prescribe drugs for uses that are not described in the product's approved labeling and for uses that differ from those tested in clinical studies and approved by the regulatory authorities, our ability to promote the products is limited to those indications that are specifically approved by the FDA. These "off-label" uses are common across medical specialties and may constitute an appropriate treatment for some patients in varied circumstances. Regulatory authorities in the United States generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications by pharmaceutical companies on the subject of off-label use or off-label information. If our promotional activities fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities. In addition, our failure to follow FDA rules and guidelines relating to promotion and advertising may cause the FDA to suspend or withdraw an approved product from the market, require a recall or corrective advertising, institute fines, or could result in disgorgement of money, operating restrictions, injunctions or civil or criminal prosecution by the government, any of which could harm our reputation and business.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of, and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidate, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and certain disabled people and introduced a reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this law provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this law and future laws could decrease the coverage and price that we will receive for any approved products. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Therefore, any limitations in reimbursement that results from the MMA may result in reductions in payments from private payors.

In March 2010, the Patient Protection and Affordable Care Act, or the ACA, became law. The ACA is a sweeping law intended 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 the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

Among the provisions of the ACA of importance to our potential product candidate are the following:

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

President Trump ran for office on a platform that supported the repeal of the ACA and one of his first actions after his inauguration was to sign an Executive Order commanding federal agencies to try to waive or delay requirements of the ACA that impose economic or regulatory burdens on states, families, the healthcare industry and others. The Executive Order also declares that the administration will seek the "prompt repeal" of the law and that the government should prepare to "afford the states more flexibility and control to create a more free and open healthcare market." At this time, the immediate impact of the Executive Order is not clear. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These new laws may result in additional reductions in Medicare and other healthcare funding.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we will receive for any approved product. Any reduction in payments from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals, if any, of our product candidates, may be. In addition, increased scrutiny by the U.S. 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 conditions and other requirements.

Public concern regarding the safety of opioid drug products such as IV Tramadol could delay or limit our ability to obtain regulatory approval, result in the inclusion of serious risk information in our labeling, negatively impact market experience, or require us to undertake other activities that may entail additional costs.

In light of widely publicized events concerning the safety risk of certain drug products, the FDA, members of Congress, the Government Accountability Office, medical professionals and the general public have raised concerns about potential controlled substance drug safety issues. These events have resulted in the withdrawal of drug products, revisions to drug labeling that further limit use of the drug products and the establishment of risk management programs. The Food and Drug Administration Amendments Act of 2007, or FDAAA, grants significant expanded authority to the FDA, much of which is aimed at improving the safety of drug products before and after approval. In particular, the new law authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information and require risk evaluation and mitigation strategies for certain drugs, including certain currently approved drugs. It also significantly expands the federal government's clinical trial registry and results databank, which we expect will result in significantly increased government oversight of clinical trials. Under the FDAAA, companies that violate these and other provisions of the new law are subject to substantial civil monetary penalties, among other regulatory, civil and criminal penalties. The increased attention to drug safety issues may result in a more cautious approach by the FDA in its review of data from our clinical trials. Data from clinical trials may receive greater scrutiny, particularly with respect to safety, which may make the FDA or other regulatory authorities more likely to require additional preclinical studies or clinical trials. If the FDA requires us to conduct additional preclinical studies or clinical trials prior to approving IV Tramadol, our ability to obtain approval of this product candidate will be delayed. If the FDA requires us to provide additional clinical or preclinical data following the approval of IV Tramadol, the indications for which this product candidate is approved may be limited or there may be specific warnings or limitations on production dosing, and our efforts to commercialize IV Tramadol may be otherwise adversely impacted.

Rising public, medical, Congressional, and agency concern around the prescription of controlled substance drug products to patients and a growing movement to reduce the use of opioid drug products, to develop abuse-deterrent products, and to prevent dependence also could negatively impact our ability to commercialize and generate revenue from IV Tramadol if it is approved for marketing in the United States.

If the DEA decides to reschedule Tramadol from a Schedule IV controlled substance to a more restrictive Schedule, IV Tramadol could lose its competitive advantage, and our related clinical development and regulatory approval could be delayed or prevented.

In July 2014, the U.S. Drug Enforcement Administration, or DEA, classified Tramadol as a Schedule IV controlled substance. In comparison, other opioids, which have a high potential for abuse, are mostly classified as Schedule I and II controlled substances. If approved, IV Tramadol will be the only Schedule IV intravenous opioid on the market. However, in the current environment where the opioid epidemic is a recognized problem in the United States, there is a possibility that the DEA might reschedule Tramadol as a Schedule I, II or III controlled substance. Such a rescheduling would severely impair IV Tramadol's current competitive advantage over traditional opioids and may affect our ability to market IV Tramadol as a safe alternative pain management product.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. Some of our competitors have ongoing clinical trials for product candidates that treat the same indications as

our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. Available therapies for the indications we are pursuing can also affect enrollment in our clinical trials. Patient enrollment is affected by other factors including, but not necessarily limited to:

- the severity of the disease under investigation;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidate or future product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

We expect intense competition for IV Tramadol, and new products may emerge that provide different or better therapeutic alternatives for our targeted indications.

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of IV Tramadol from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. There can be no assurance that developments by others will not render IV Tramadol obsolete or noncompetitive. Furthermore, new developments, including the development of other drug technologies and methods of preventing the incidence of disease, occur in the pharmaceutical industry at a rapid pace. These developments may render IV Tramadol obsolete or noncompetitive.

IV Tramadol will compete with well-established products with similar indications. Competing products available for the management of pain include Ofirmev (IV acetaminophen) and IV formulations of NSAIDs such as Dyloject (diclofenac), Toradol (ketorolac), and Caldolor (ibuprofen). In addition, we also expect to compete with agents such as Exparel, a liposome injection of bupivacaine indicated for administration into the surgical site to produce postsurgical analgesia. In addition to approved products, there are a number of product candidates in development for the management of acute pain. The late-stage pain development pipeline is replete with reformulations and fixed-dose combination products of already available therapies. Among specific drug classes, opioid analgesics and NSAIDs represent the greatest number of agents in development. Most investigational opioids that have reached the later stages of clinical development are new formulations of already marketed opioids. Likewise, investigational NSAIDs — mostly lower dose injectable reformulations of already approved compounds — are another significant area of late-stage drug development in the postoperative pain space. There are also several agents with novel mechanisms in clinical development, such as CR845 (Cara Therapeutics, Inc.) and TRV130 (Trevena, Inc.).

Competitors may seek to develop alternative formulations of IV centrally acting synthetic opioid analgesics for our targeted indications that do not directly infringe on our in-licensed patent rights. The commercial opportunity for IV Tramadol could be significantly harmed if competitors are able to develop alternative formulations outside the scope of our in-licensed patents. Compared to us, many of our potential competitors have substantially greater:

- capital resources;
- development resources, including personnel and technology;
- clinical trial experience;
- regulatory experience;
- expertise in prosecution of intellectual property rights; and
- manufacturing, distribution and sales and marketing experience.

As a result of these factors, our competitors may obtain regulatory approval of their products more rapidly than we are able to or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize IV Tramadol. Our competitors may also develop drugs that are more effective, safe, useful and less costly than ours and may be more successful than us in manufacturing and marketing their products.

If IV Tramadol does not achieve broad market acceptance, the revenues that we generate from its sales will be limited.

The commercial success of IV Tramadol, if approved, will depend upon its acceptance by the medical community, our ability to ensure that the drug is included in hospital formularies, and coverage and reimbursement for IV Tramadol by third party payors, including government payors. The degree of market acceptance of IV Tramadol or any other product candidate we may license or acquire will depend on a number of factors, including, but not necessarily limited to:

- the efficacy and safety as demonstrated in clinical trials;
- the timing of market introduction of such product candidate as well as competitive products;
- the clinical indications for which the drug is approved;
- acceptance by physicians, major operators of cancer clinics and patients of the drug as a safe and effective treatment;
- the safety of such product candidate seen in a broader patient group, including its use outside the approved indications;
- the availability, cost and potential advantages of alternative treatments, including less expensive generic drugs;
- the availability of adequate reimbursement and pricing by third party payors and government authorities;
- the relative convenience and ease of administration of the product candidate for clinical practices;
- the product labeling or product insert required by the FDA or regulatory authority in other countries, including any contradictions, warnings, drug interactions, or other precautions;
- the approval, availability, market acceptance and reimbursement for a companion diagnostic, if any;
- the prevalence and severity of adverse side effects;
- the effectiveness of our sales and marketing efforts;

- limitations or warnings contained in the product's FDA-approved labeling;
- changes in the standard of care for the targeted indications for our product candidate or future product candidates, which could reduce the marketing impact of any superiority claims that we could make following FDA approval; and
- potential advantages over, and availability of, alternative treatments.

If any product candidate that we develop does not provide a treatment regimen that is as beneficial as, or is not perceived as being as beneficial as, the current standard of care or otherwise does not provide patient benefit, that product candidate, if approved for commercial sale by the FDA or other regulatory authorities, likely will not achieve market acceptance. Our ability to effectively promote and sell IV Tramadol and any other product candidates we may license or acquire in the hospital marketplace will also depend on pricing and cost effectiveness, including our ability to produce a product at a competitive price and achieve acceptance of the product onto hospital formularies, as well as our ability to obtain sufficient third party coverage or reimbursement. Since many hospitals are members of group purchasing organizations, which leverage the purchasing power of a group of entities to obtain discounts based on the collective buying power of the group, our ability to attract customers in the hospital marketplace will also depend on our ability to effectively promote our product candidates to group purchasing organizations. We will also need to demonstrate acceptable evidence of safety and efficacy, as well as relative convenience and ease of administration. Market acceptance could be further limited depending on the prevalence and severity of any expected or unexpected adverse side effects associated with our product candidates. If our product candidates are approved but do not achieve an adequate level of acceptance by physicians, health care payors and patients, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, our efforts to educate the medical community and third party payors on the benefits of our product candidates may require significant resources and may never be successful.

If the government or third party payors fail to provide adequate coverage and payment rates for IV Tramadol or any future products we may license or acquire, if any, or if hospitals choose to use therapies that are less expensive, our revenue and prospects for profitability will be limited.

In both domestic and foreign markets, our sales of any future products will depend in part upon the availability of coverage and reimbursement from third party payors. Such third party payors include government health programs such as Medicare, managed care providers, private health insurers and other organizations. In particular, many U.S. hospitals receive a fixed reimbursement amount per procedure for certain surgeries and other treatment therapies they perform. Because this amount may not be based on the actual expenses the hospital incurs, hospitals may choose to use therapies which are less expensive when compared to our product candidate or future product candidates. Accordingly, IV Tramadol or any other product candidates that we may in-license or acquire, if approved, will face competition from other therapies and drugs for these limited hospital financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of hospitals, other target customers and their third party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

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

We currently do not have a marketing or sales organization for the marketing, sales and distribution of pharmaceutical products. In order to commercialize any product candidate that receives marketing approval, we would need to build marketing, sales, distribution, managerial

and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In the event of successful development and regulatory approval of IV Tramadol or another product candidate, we expect to build a targeted specialist sales force to market or co-promote the product. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our future products, if any, on our own include, but are not necessarily limited to:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary or other products to be offered by sales personnel, which may put us at a competitive disadvantage from the perspective of sales efficiency relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

As an alternative to establishing our own sales force, we may choose to partner with third parties that have well-established direct sales forces to sell, market and distribute our products. There are risks involved with partnering with third party sales forces, including ensuring adequate training on the product, regulatory, and compliance requirements associated with promotion of the product.

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or complying with applicable regulatory requirements.

We rely on third party contract research organizations and clinical research organizations to conduct some of our preclinical studies and all of our clinical trials for IV Tramadol and for any future product candidates. We expect to continue to rely on third parties, such as contract research organizations, clinical research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct some of our preclinical studies and all of our clinical trials. The agreements with these third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, that could delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our legal and regulatory product development responsibilities. For example, we will remain responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial and for ensuring that our preclinical studies are conducted in accordance with good laboratory practice, or GLP, as appropriate. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of our clinical research organizations fail to comply with applicable GCPs, the clinical data generated in our

clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

The third parties with whom we have contracted to help perform our preclinical studies or clinical trials may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our preclinical studies or clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

If any of our relationships with these third party contract research organizations or clinical research organizations terminates, we may not be able to enter into arrangements with alternative contract research organizations or clinical research organizations or to do so on commercially reasonable terms. Switching or adding additional contract research organizations or clinical research organizations involves additional cost and requires extensive training and management time and focus. In addition, there is a natural transition period when a new contract research organization or clinical research organization commences work. As a result, delays could occur, which could compromise our ability to meet our desired development timelines. Though we carefully manage our relationships with our contract research organizations or clinical research organizations, there can be no assurance that we will not encounter challenges or delays in the future.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We also expect to rely on third party manufacturers or third party collaborators for the manufacture of commercial supply of any product candidates for which our collaborators or we obtain marketing approval. We may be unable to establish any agreements with third party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third party manufacturers, reliance on third party manufacturers entails additional risks, including, but not necessarily limited to:

- reliance on the third party for regulatory compliance and quality assurance;
- raw material or active ingredient shortages from suppliers the third party has qualified for our product;
- the possible breach of the manufacturing agreement by the third party;

- manufacturing delays if our third party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturers for compliance with cGMP regulations for manufacture of our product candidates. Third party manufacturers may not be able to comply with the cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

IV Tramadol and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. We may incur added costs and delays in identifying and qualifying any replacement manufacturers.

The U.S. Drug Enforcement Administration, or the DEA, restricts the importation of a controlled substance finished drug product when the same substance is commercially available in the United States, which could reduce the number of potential alternative manufacturers for IV Tramadol.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential product revenue.

We rely on clinical data and results obtained by third parties that could ultimately prove to be inaccurate or unreliable.

As part of our strategy to mitigate development risk, we seek to develop product candidates with validated mechanisms of action and we utilize biomarkers to assess potential clinical efficacy early in the development process. This strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable. Further, such clinical data and results may be based on products or product candidates that are significantly different from our product candidate or future product candidates. If the third party data and results we rely upon prove to be inaccurate, unreliable or not applicable to our product candidate or future product candidate, we could make inaccurate assumptions and conclusions about our product candidates and our research and development efforts could be compromised and called into question during the review or any marketing applications we submit.

If we breach the agreement under which we license rights to IV Tramadol, we could lose the ability to continue to develop and commercialize this product candidate.

In February 2015, Fortress obtained an exclusive license to IV Tramadol for the U.S. market from Revogenex Ireland Ltd., or Revogenex, pursuant to the License Agreement; Fortress transferred the License Agreement to us. Because we have in-licensed the rights to this product candidate from a third party, if there is any dispute between us and our licensor regarding our rights under our License Agreement, our ability to develop and commercialize this product candidate may be adversely affected. Any uncured, material breach under our License Agreement could result in our loss of exclusive rights to our product candidate and may lead to a complete termination of our related product development efforts.

We may not be able to manage our business effectively if we are unable to attract and retain key personnel.

We may not be able to attract or retain qualified management and commercial, scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our employees, consultants, or third party partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees, consultants, or third party partners could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee, consultant, or third party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

We face potential product liability exposure, and if successful claims are brought against us, we may incur substantial liability for IV Tramadol or other product candidates we may license or acquire and may have to limit their commercialization.

The use of IV Tramadol and any other product candidates we may license or acquire in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical 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 or a breach of warranties. Product liability claims might be brought against us by consumers, health care providers or others using, administering or selling our

products. If we cannot successfully defend ourselves against these claims, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- decreased demand for any product candidates or products that we may develop;
- initiation of investigations by regulators;
- impairment of our business reputation;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- loss of revenues;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize our product candidate or future product candidates.

We will obtain limited product liability insurance coverage for our upcoming clinical trials. However, our insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. When needed, we intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for our product candidate in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to fall and, if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

Our future growth depends on our ability to identify and acquire or in-license products and if we do not successfully identify and acquire or in-license related product candidates or integrate them into our operations, we may have limited growth opportunities.

An important part of our business strategy is to continue to develop a pipeline of product candidates by acquiring or in-licensing products, businesses or technologies that we believe are a strategic fit with our focus on the hospital marketplace. Future in-licenses or acquisitions, however, may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- difficulty or inability to secure financing to fund development activities for such acquired or in-licensed technologies in the current economic environment;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;

- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

We have limited resources to identify and execute the acquisition or in-licensing of third party products, businesses and technologies and integrate them into our current infrastructure. In particular, we may compete with larger pharmaceutical companies and other competitors in our efforts to establish new collaborations and in-licensing opportunities. These competitors likely will have access to greater financial resources than us and may have greater expertise in identifying and evaluating new opportunities. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts.

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.

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

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 harm 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. Although we believe that the safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental 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 for failure to comply with such laws and regulations.

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. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Any system failure, accident or security breach that causes interruptions in our operations could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed clinical trials for IV Tramadol 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 or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liability and the further development of our product candidate may be delayed.

Risks Related to Intellectual Property

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

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection in the United States with respect to IV Tramadol or any other product candidates that we may license or acquire and the methods we use to manufacture them, as well as successfully defending these patents and trade secrets against third party challenges. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates. We will only be able to protect our technologies from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. If our licensors or we fail to obtain or maintain patent protection or trade secret protection for IV Tramadol or any other product candidate we may license or acquire, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and achieve profitability. Moreover, should we enter into other collaborations we may be required to consult with or cede control to collaborators regarding the prosecution, maintenance and enforcement of our patents. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, no consistent policy regarding the breadth of claims allowed in pharmaceutical or biotechnology patents has emerged to date in the United States. The patent situation outside the United States is even more uncertain. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after a first filing, or in some cases at all. Therefore, we cannot know with certainty whether we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In the event that a third party has also filed a U.S. patent application relating to our product candidates or a similar invention, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention in the United States. The costs of these proceedings could be substantial and it is possible that our efforts would

be unsuccessful, resulting in a material adverse effect on our U.S. patent position. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. For example, the federal courts of the United States have taken an increasingly dim view of the patent eligibility of certain subject matter, such as naturally occurring nucleic acid sequences, amino acid sequences and certain methods of utilizing same, which include their detection in a biological sample and diagnostic conclusions arising from their detection. Such subject matter, which had long been a staple of the biotechnology and biopharmaceutical industry to protect their discoveries, is now considered, with few exceptions, ineligible in the first place for protection under the patent laws of the United States. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents (if any) or in those licensed from third parties.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The USPTO recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third party preissuance submission of prior art to the USPTO, or become involved in opposition, derivation, reexamination, *inter parties* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, patent office trial, proceeding or litigation could reduce the scope of, render unenforceable, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent does not foreclose challenges to its inventorship, scope, validity or enforceability. Therefore, our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned

and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

The patent rights that we have in-licensed covering the infusion time and pharmacokinetics, or PK, profile for IV Tramadol are limited to a specific IV formulation of centrally acting synthetic opioid analgesic, and our market opportunity for this product candidate may be limited by the lack of patent protection for the active ingredient itself and other formulations that may be developed by competitors.

The active ingredients in IV Tramadol have been generic in the United States for a number of years. While we believe that the patent estate covering IV Tramadol (including but not limited to U.S. Patent Nos. 8,895,622; 9,561,195 and 9,566,253) provides strong protection, our market opportunity would be limited if a generic manufacturer could obtain regulatory approval for another IV formulation of tramadol and commercialize it without infringing on our patent.

Because it is difficult and costly to protect our proprietary rights, we may not be able to ensure their protection.

The degree of future protection for our proprietary rights is uncertain, because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- our licensors might not have been the first to make the inventions covered by each of our pending patent applications and issued patents;
- our licensors might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate our product candidate or any future product candidates technologies;
- it is possible that none of the pending patent applications licensed to us will result in issued patents;
- the issued patents covering our product candidate or any future product candidates may not provide a basis for market exclusivity for active products, may not provide us with any competitive advantages, or may be challenged by third parties;
- we may not develop additional proprietary technologies that are patentable; or
- patents of others may have an adverse effect on our business.

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

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or 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 proceeding could put one or more of our patents at risk of being invalidated, rendered unenforceable, or interpreted narrowly.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in any litigation would harm our business.

Our ability to develop, manufacture, market and sell IV Tramadol or any other product candidates that we may license or acquire depends upon our ability to avoid infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent

applications, which are owned by third parties, exist in the general fields of pain treatment and cover the use of numerous compounds and formulations in our targeted markets. Because of the uncertainty inherent in any patent or other litigation involving proprietary rights, we and our licensors may not be successful in defending intellectual property claims by third parties, which could have a material adverse effect on our results of operations. Regardless of the outcome of any litigation, defending the litigation may be expensive, time-consuming and distracting to management. In addition, because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that IV Tramadol may infringe. There could also be existing patents of which we are not aware that IV Tramadol may inadvertently infringe.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we infringe on their patents or misappropriated their technology, we could face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, can be expensive and time consuming to litigate and can divert management's attention from our core business;
- substantial damages for past infringement which we may have to pay if a court decides that our product infringes on a competitor's patent;
- a court prohibiting us from selling or licensing our product unless the patent holder licenses the patent to us, which it would not be required to do;
- if a license is available from a patent holder, we may have to pay substantial royalties or grant cross licenses to our patents; and
- redesigning our processes so they do not infringe, which may not be possible or could require substantial funds and time.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights that are important or necessary to the development and commercialization of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are currently party to a license agreement for IV Tramadol. In the future, we may become party to licenses that are important for product development and commercialization. If we fail to comply with our obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product or utilize any technology that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially and adversely affect the value of a product candidate being developed under any such agreement or could restrict our drug discovery activities. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

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

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. 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 are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for our product candidate or future product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position, particularly where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We limit disclosure of such trade secrets where possible but we also seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who do have access to them, such as our employees, our licensors, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and may unintentionally or willfully disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Our Finances and Capital Requirements

We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future, and may never achieve or maintain profitability.

We are an emerging growth company with a limited operating history. We have focused primarily on in-licensing and developing IV Tramadol, with the goal of supporting regulatory approval for this product candidate. We have incurred losses since our inception in February 2015.

These losses, among other things, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect to continue to incur significant operating losses for the foreseeable future. We also do not anticipate that we will achieve profitability for a period of time after generating material revenues, if ever. If we are unable to generate revenues, we will not become profitable and may be unable to continue operations without continued funding. Because of the numerous risks and uncertainties associated with developing pharmaceutical products, we are unable to predict the timing or amount of increased expenses or when or if, we will be able to achieve profitability. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially if:

- IV Tramadol or other product candidates are approved for commercial sale, due to the necessity in establishing adequate commercial infrastructure to launch this product candidate without substantial delays, including hiring sales and marketing personnel and contracting with third parties for warehousing, distribution, cash collection and related commercial activities;
- we are required by the FDA, or foreign regulatory authorities, to perform studies in addition to those currently expected;
- there are any delays in completing our clinical trials or the development of any of our product candidates;
- we execute other collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- there variations in the level of expenses related to our future development programs;
- there are any product liability or intellectual property infringement lawsuits in which we may become involved; and
- there are any regulatory developments affecting IV Tramadol or the product candidates of our competitors.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from our development stage product, and we do not know when, or if, we will generate any revenue. Our ability to generate revenue depends on a number of factors, including, but not limited to, our ability to:

- obtain regulatory approval for IV Tramadol, or any other product candidates that we may license or acquire;
- manufacture commercial quantities of IV Tramadol or other product candidates, if approved, at acceptable cost levels; and
- develop a commercial organization and the supporting infrastructure required to successfully market and sell IV Tramadol or other product candidates, if approved.

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

Our short operating history makes it difficult to evaluate our business and prospects.

We were incorporated on February 9, 2015, and have only been conducting operations with respect to IV Tramadol since February 17, 2015. We have not yet demonstrated an ability to successfully complete clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about

our future performance may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to expand our capabilities to support commercial activities. We may not be successful in adding such capabilities.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any past quarterly period as an indication of future operating performance.

We do not have any products that are approved for commercial sale and therefore do not expect to generate any revenues from product sales in the foreseeable future, if ever.

We have not generated any product related revenues to date, and do not expect to generate any such revenues for at least the next several years, if at all. To obtain revenues from sales of our product candidates, we must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing and marketing products with commercial potential. We may never succeed in these activities, and we may not generate sufficient revenues to continue our business operations or achieve profitability.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all. If we fail to raise the necessary additional capital, we may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our product development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. We expect to significantly increase our spending to advance the preclinical and clinical development of IV Tramadol and launch and commercialize any additional product candidates for which we receive regulatory approval, including building our own commercial organizations to address certain markets. We will require additional capital for the further development and commercialization of our product candidates, as well as to fund our other operating expenses and capital expenditures, and cannot provide any assurance that we will be able to raise funds to complete the development of our product.

We cannot be certain that additional funding will be available on acceptable terms, or at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates. We may also seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available. Any of these events could significantly harm our business, financial condition and prospects.

Our future funding requirements will depend on many factors, including, but not limited to:

- the timing, design and conduct of, and results from, preclinical and clinical trials for our product candidates;
- the potential for delays in our efforts to seek regulatory approval for our product candidates, and any costs associated with such delays;
- the costs of establishing a commercial organization to sell, market and distribute our product candidates;
- the rate of progress and costs of our efforts to prepare for the submission of an NDA for any product candidates that we may in-license or acquire in the future, and the potential that we may need to conduct additional clinical trials to support applications for regulatory approval;

- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights associated with our product candidates, including any such costs we may be required to expend if our licensors are unwilling or unable to do so;
- the cost and timing of securing sufficient supplies of our product candidates from our contract manufacturers for clinical trials and in preparation for commercialization;
- the effect of competing technological and market developments;
- the terms and timing of any collaborative, licensing, co-promotion or other arrangements that we may establish;
- if one or more of our product candidates are approved, the potential that we may be required to file a lawsuit to defend our patent rights or regulatory exclusivities from challenges by companies seeking to market generic versions of one or more of our product candidates; and
- the success of the commercialization of one or more of our product candidates.

Future capital requirements will also depend on the extent to which we acquire or invest in additional complementary businesses, products and technologies.

In order to carry out our business plan and implement our strategy, we anticipate that we will need to obtain additional financing from time to time and may choose to raise additional funds through strategic collaborations, licensing arrangements, public or private equity or debt financing, bank lines of credit, asset sales, government grants, or other arrangements. We cannot be sure that any additional funding, if needed, will be available on terms favorable to us or at all. Furthermore, any additional equity or equity-related financing may be dilutive to our stockholders, and debt or equity financing, if available, may subject us to restrictive covenants and significant interest costs. If we obtain funding through a strategic collaboration or licensing arrangement, we may be required to relinquish our rights to certain of our product candidates or marketing territories.

Our inability to raise capital when needed would harm our business, financial condition and results of operations, and could cause our stock value to decline or require that we wind down our operations altogether.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish proprietary rights.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, grants and license and development agreements in connection with any collaborations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

We intend to become a listed and traded public company. As a public company, we will incur significant legal, accounting and other expenses under the Sarbanes-Oxley Act of 2002, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and the rules of any stock exchange on which we may become listed. These rules impose various requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and appropriate corporate governance practices. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified persons to serve on our Board of Directors, our Board committees or as executive officers.

The Sarbanes-Oxley Act of 2002 requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. As a result, we are required to periodically perform an evaluation of our internal controls over financial reporting to allow management to report on the effectiveness of those controls, as required by Section 404 of the Sarbanes-Oxley Act. Additionally, our independent auditors are required to perform a similar evaluation and report on the effectiveness of our internal controls over financial reporting. These efforts to comply with Section 404 and related regulations have required, and continue to require, the commitment of significant financial and managerial resources. While we anticipate maintaining the integrity of our internal controls over financial reporting and all other aspects of Section 404, we cannot be certain that a material weakness will not be identified when we test the effectiveness of our control systems in the future. If a material weakness is identified, we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources, costly litigation or a loss of public confidence in our internal controls, which could have an adverse effect on the market price of our stock.

We are an "emerging growth company" and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our securities less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act. We will remain an "emerging growth company" for up to five years. We may take advantage of these provisions until the earlier of (i) the last day of our fiscal year following the fifth anniversary of the closing of this offering (ii) the last day of the fiscal year (a) in which we have total annual gross revenue of at least $1.0 billion or (b) in which we are deemed to be a large accelerated filer, which means the market value of our equity securities that is held by non-affiliates exceeds $700 million as of the last business day of our most recently completed second fiscal quarter, and (iii) the date on which we have issued more than $1.0 billion of non-convertible debt in any three-year period. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and being exempt from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. Additionally, as an emerging growth company, we have elected to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. As such, our financial statements may not be comparable to companies that comply with public company effective dates. We cannot predict if investors will find our shares

less attractive because we may rely on these provisions. If some investors find our shares less attractive as a result, there may be a less active trading market for our shares and our share price may be more volatile.

Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturn.

Our results of operations could be materially negatively affected by economic conditions generally, both in the United States and elsewhere around the world. Continuing concerns over inflation, energy costs, geopolitical issues, the availability and cost of credit, the U.S. mortgage market and residential real estate market in the United States have contributed to increased volatility and diminished expectations for the economy and the markets going forward. These factors, combined with volatile oil prices, declining business and consumer confidence and increased unemployment, have precipitated an economic recession and fears of a possible depression. Domestic and international equity markets continue to experience heightened volatility and turmoil. These events and the continuing market upheavals may have an adverse effect on us. In the event of a continuing market downturn, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may further decline.

Our independent registered public accounting firm has expressed substantial doubt about our ability to continue as a going concern.

The report of our independent auditors dated March 6, 2017, on our financial statements for the periods ended December 31, 2016 and 2015, included an explanatory paragraph indicating that there is substantial doubt about our ability to continue as a going concern. The substantial doubts are based on our working capital deficit of approximately $6.2 million and $2.4 million, respectively, and our stockholders' deficit of approximately $8.2 million and $5.2 million, respectively, and we have incurred losses of approximately $3.2 million for the year ended December 31, 2016 and $5.2 million for the period from inception to December 31, 2015. Further, we expect to continue to incur significant costs in pursuit of our financing plans and product development. Our ability to continue as a going concern will be determined by our ability to raise additional capital in the form of debt or equity financing. Our financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or amounts and classification of liabilities that might be necessary should we be unable to continue as a going concern.

Risks Relating to Securities Markets and Investment in Our Stock

There is not now and there may not ever be an active market for our common stock. There are restrictions on the transferability of these securities.

There currently is no market for our common stock and, except as otherwise described herein, we have no plans to file any registration statement or otherwise attempt to create a market for the shares. Even if an active market develops for the shares, Rule 144, which provides for an exemption from the registration requirements under the Securities Act of 1933, as amended, or the Securities Act, under certain conditions, requires, among other conditions, a holding period prior to the resale (in limited amounts) of securities acquired in a non-public offering without having to satisfy the registration requirements under the Securities Act. There can be no assurance that we will fulfill any reporting requirements in the future under the Securities Exchange Act of 1934, as amended, or the Exchange Act, or disseminate to the public any current financial or other information concerning us, as is required by Rule 144 as part of the conditions of its availability.

Our stock may be subject to substantial price and volume fluctuations due to a number of factors, many of which are beyond our control and may prevent our stockholders from reselling our common stock at a profit.

The market prices for securities of biotechnology and pharmaceutical companies have historically been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies.

The market price of our common stock is likely to be highly volatile and may fluctuate substantially due to many factors, including:

- announcements concerning the progress of our efforts to obtain regulatory approval for and commercialize IV Tramadol or future product candidates, including any requests we receive from the FDA for additional studies or data that result in delays in obtaining regulatory approval or launching this product candidate, if approved;
- market conditions in the pharmaceutical and biotechnology sectors or the economy as a whole;
- price and volume fluctuations in the overall stock market;
- the failure of IV Tramadol or future product candidates, if approved, to achieve commercial success;
- announcements of the introduction of new products by us or our competitors;
- developments concerning product development results or intellectual property rights of others;
- litigation or public concern about the safety of our potential products;
- actual fluctuations in our quarterly operating results, and concerns by investors that such fluctuations may occur in the future;
- deviations in our operating results from the estimates of securities analysts or other analyst comments;
- additions or departures of key personnel;
- health care reform legislation, including measures directed at controlling the pricing of pharmaceutical products, and third party coverage and reimbursement policies;
- developments concerning current or future strategic collaborations; and
- discussion of us or our stock price by the financial and scientific press and in online investor communities.

Following completion of our proposed initial public offering, Fortress will continue to control a voting majority of our common stock, whose interests may differ from yours.

Pursuant to the terms of the Class A Preferred Stock held by Fortress, Fortress will be entitled to cast, for each share of Class A Preferred Stock held by Fortress, the number of votes that is equal to 1.1 times a fraction, the numerator of which is the sum of (A) the aggregate number of shares of outstanding common stock and (B) the whole shares of common stock into which the shares of outstanding the Class A Preferred Stock are convertible and the denominator of which is the aggregate number of shares of outstanding Class A Preferred Stock, or the Class A Preferred Stock Ratio. Thus, Fortress will at all times have voting control of us. Further, for a period of ten years from the date of the first issuance of shares of Class A Preferred Stock, the holders of record of the shares of Class A Preferred Stock (or other capital stock or securities issued upon conversion of or in exchange for the Class A Preferred Stock), exclusively and as a separate class, shall be entitled to appoint or elect the majority of our directors. This concentration of voting power may delay, prevent or deter a change in control, even when such a change may be in the best interests of all

stockholders, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of us or our assets, and might affect the prevailing market price of our common stock.

Fortress has the right to receive a significant grant of shares of our common stock annually, which will result in the dilution of your holdings of common stock upon each grant, which could reduce their value.

Under the terms of the Amended and Restated Founders Agreement, which became effective September 13, 2016, Fortress will receive a grant of shares of our common stock equal to 2.5% of the gross amount of any equity or debt financing. Additionally, the holders of Class A Preferred Stock, as a class, will receive an annual dividend, payable in shares of common stock in an amount equal to 2.5% of our fully-diluted outstanding capital stock as of the business day immediately prior to the date such dividend is payable. Fortress currently owns all outstanding shares of Class A Preferred Stock. These share issuances to Fortress and any other holder of Class A Preferred Stock will dilute your holdings in our common stock and, if our value has not grown proportionately over the prior year, would result in a reduction in the value of your shares. The Amended and Restated Founders Agreement has a term of 15 years and renews automatically for subsequent one-year periods unless terminated by Fortress or upon a Change in Control (as defined in the Amended and Restated Founders Agreement).

We are a "controlled company" within the meaning of NASDAQ listing standards and, as a result, qualify for, and rely on, exemptions from certain corporate governance requirements. You will not have the same protections afforded to stockholders of companies that are subject to such requirements.

We are a "controlled company" within the meaning of NASDAQ listing standards. Under these rules, a company of which more than 50% of the voting power is held by an individual, a group or another company is a "controlled company" and may elect not to comply with certain corporate governance requirements of NASDAQ, including (i) the requirement that a majority of the Board of Directors consist of independent directors, (ii) the requirement that we have a nominating and corporate governance committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities and (iii) the requirement that we have a compensation committee that is composed entirely of independent directors with a written charter addressing the committee's purpose and responsibilities. We intend to rely on some or all of these exemptions.

Accordingly, you will not have the same protections afforded to stockholders of companies subject to all of the corporate governance requirements of NASDAQ.

Investors in this offering will suffer immediate and substantial dilution of their investment.

If you purchase common stock in this offering, you will pay more for your shares than our as adjusted net tangible book value per share. Based upon an assumed initial public offering price of $ per share, the midpoint of the price range on the cover page of this prospectus, you will incur immediate and substantial dilution of $ per share, representing the difference between our assumed initial public offering price and our as adjusted net tangible book value per share. Based upon the assumed initial public offering price of $ per share, purchasers of common stock in this offering will have contributed approximately % of the aggregate purchase price paid by all purchasers of our stock but will own only approximately % of our common stock outstanding after this offering.

We might have received better terms from unaffiliated third parties than the terms we receive in our agreements with Fortress.

The agreements we entered into with Fortress in connection with the separation include the Management Services Agreement, or the MSA, and the Founders Agreement. While we believe the terms of these agreements are reasonable, they might not reflect terms that would have resulted

from arm's-length negotiations between unaffiliated third parties. The terms of the agreements relate to, among other things, payment of a royalty on product sales and the provision of employment and transition services. We might have received better terms from third parties because, among other things, third parties might have competed with each other to win our business.

The ownership by our executive officers and some of our directors of shares of equity securities of Fortress and/or rights to acquire equity securities of Fortress might create, or appear to create, conflicts of interest.

Because of their current or former positions with Fortress, some of our executive officers and directors own shares of Fortress common stock and/or options to purchase shares of Fortress common stock. Their individual holdings of common stock and/or options to purchase common stock of Fortress may be significant compared to their total assets. Ownership by our directors and officers, after our separation, of common stock and/or options to purchase common stock of Fortress create might appear to create conflicts of interest when these directors and officers are faced with decisions that could have different implications for Fortress than for us. For instance, and by way of example, if there were to be a dispute between Fortress and us regarding the calculation of the royalty fee due to Fortress under the terms of the Founders Agreement, then certain of our senior employees may have and will appear to have a conflict of interest with regard to the outcome of such dispute.

The dual roles of our officers and directors who also serve in similar roles with Fortress could create a conflict of interest and will require careful monitoring by our independent directors.

We share some directors with Fortress, and in addition, under the Management Services Agreement, we will also share some officers with Fortress. This could create conflicts of interest between the two companies in the future. While we believe that the Founders Agreement and the Management Services Agreement were negotiated by independent parties on both sides on arm's length terms, and the fiduciary duties of both parties were thereby satisfied, in the future situations may arise under the operation of both agreements that may create a conflict of interest. We will have to be diligent to ensure that any such situation is resolved by independent parties. In particular, under the Management Services Agreement, Fortress and its affiliates are free to pursue opportunities which could potentially be of interest to us, and they are not required to notify us prior to pursuing the opportunity. Any such conflict of interest or pursuit by Fortress of a corporate opportunity independent of us could expose us to claims by our investors and creditors, and could harm our results of operations.

We may become involved in securities class action litigation that could divert management's attention and harm our business.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the common stock of biotechnology and pharmaceutical companies. These broad market fluctuations may cause the market price of our stock to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharmaceutical companies have experienced significant stock price volatility in recent years. We may become involved in this type of litigation in the future. Litigation often is expensive and diverts management's attention and resources, which could adversely affect our business.

SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

Certain matters discussed in this prospectus may constitute forward-looking statements for purposes of the Securities Act and the Exchange Act, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from the future results, performance or achievements expressed or implied by such forward-looking statements. The words "anticipate," "believe," "estimate," "may," "expect" and similar expressions are generally intended to identify forward-looking statements. Our actual results may differ materially from the results anticipated in these forward-looking statements due to a variety of factors, including, without limitation, those discussed under the captions "Risk Factors," and elsewhere in this prospectus. All written or oral forward-looking statements attributable to us are expressly qualified in their entirety by these cautionary statements. Such forward-looking statements include, but are not limited to, statements about our:

- expectations for the clinical and preclinical development, manufacturing, regulatory approval, and commercialization of our pharmaceutical product candidate or any other products we may acquire or in-license;
- expectations for increases or decreases in expenses;
- use of clinical research centers and other contractors;
- expectations for incurring capital expenditures to expand our research and development and manufacturing capabilities;
- expectations for generating revenue or becoming profitable on a sustained basis;
- expectations or ability to enter into marketing and other partnership agreements;
- expectations or ability to enter into product acquisition and in-licensing transactions;
- expectations or ability to build our own commercial infrastructure to manufacture, market and sell our drug candidates;
- acceptance of our products by doctors, patients or payors;
- ability to compete against other companies and research institutions;
- ability to secure adequate protection for our intellectual property;
- ability to attract and retain key personnel;
- availability of reimbursement for our products;
- estimates of the sufficiency of our existing cash and cash equivalents and investments to finance our operating requirements, including expectations regarding the value and liquidity of our investments;
- the volatility of our stock price;
- expected losses; and
- expectations for future capital requirements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations.

You should read this prospectus and the documents that we reference in this prospectus and have filed with the SEC as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of the shares of our common stock in this offering will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares in full, based upon an assumed initial public offering price of $ per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of shares in the number of shares offered by us would increase (decrease) the net proceeds to us from this offering by approximately $ million, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We do not expect that a change in the initial public offering price or the number of shares by these amounts would have a material effect on our uses of the proceeds from this offering, although it may accelerate the time at which we will need to seek additional capital.

We currently estimate that we will use the net proceeds from this offering as follows:

- approximately $30 million to fund our continued clinical research and development initiatives in connection with IV Tramadol;
- approximately $6 million to pay off our debts to Fortress and NSC; and
- the remainder, if any, to fund general corporate initiatives, including preliminary commercial preparation, and for general corporate purposes.

These expected uses represent our intentions based on our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The timing and amounts of our actual expenditures will depend on several factors, including data results, progression of our clinical development programs as well as our joint collaborations, and any unforeseen cash needs.

As of the date of this prospectus, we cannot predict with absolute certainty all of the particular uses for the net proceeds to us from the offering. Accordingly, our management will have broad discretion in the application of proceeds. Pending the uses described above, we will invest the net proceeds in short-term and long-term, investment grade, interest-bearing securities.

DIVIDEND POLICY

We have never paid cash dividends on any of our capital stock and currently intend to retain our future earnings, if any, to fund the development and growth of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and capitalization as of December 31, 2016:

- on an actual basis;
- on a pro forma basis to give effect to:
  - the issuance of shares of our common stock upon the closing of this offering as a result of the conversion of the 2016 convertible notes in the principal amount of $200,000, assuming an initial public offering price of $ per share (which is the midpoint of the price range set forth on the cover page of this prospectus), and assuming the conversion occurs on , 2017 (the expected closing date of this offering);
  - on a pro forma as adjusted basis to give further effect to the issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with "Selected Financial Data," our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus.

As of December 31, 2016

(in thousands)	**Actual**	**Pro Forma**	**Pro Forma as Adjusted (1)**
Cash and cash equivalents	$ 197	$	$
Stockholder's Deficit	197		
Preferred Stock ($0.0001 par value), 2,000,000 shares authorized			
Class A Preferred Stock, 250,000 and 0 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—		
Common Stock ($0.0001 par value), 50,000,000 shares authorized			
Class A Common Stock, 0 and 7,000,000 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—		
Common shares; 9,773,810 and 2,150,000 shares issued and outstanding as of December 31, 2016 and 2015, respectively	1		
Common stock issuable, 250,595 and 228,750 shares as of December 31, 2016 and 2015, respectively	49		
Additional paid-in capital	105		
Accumulated deficit	(8,403)		
Total stockholders' deficit	**(8,248)**		
Total capitalization	$ 197	$	$

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase (decrease) each of cash and cash equivalents, additional paid-in capital, total stockholders' equity (deficit) and total capitalization on a pro forma as adjusted basis by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions.

An increase (decrease) of one million shares in the number of shares offered by us in the assumed initial public offering would increase our net tangible book value after this offering by approximately $ million, or $ per share, and decrease the dilution per share to new investors by approximately $ per share, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The number of shares of our common stock to be outstanding after this offering is based on 10,023,810 shares of our common stock outstanding as of December 31, 2016, and excludes the following:

- 2,000,000 shares of our common stock reserved for issuance under our 2015 Incentive Plan (there have been no options granted or other securities issued under our 2015 Incentive Plan);
- shares of our common stock convertible upon the completion of our initial public offering related to the sale of convertible notes in December 2016 in the aggregate amount of $200,000; and
- shares underlying a warrant to be issued to National Securities Corporation following our initial public offering.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock immediately after the offering. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding.

Our historical net tangible book value as of December 31, 2016 was deficit of $8.4 million, or $(0.84) per share of our common stock.

After giving effect to our issuance and sale of $ million of shares of our common stock in this offering at the assumed initial offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2016, would have been $ million, or $ per share. This represents an immediate increase in as adjusted net tangible book value per share of $ to existing stockholders and immediate dilution of $ in as adjusted net tangible book value per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the offering price per share paid by new investors. The following table illustrates this dilution on a per share basis.

Assumed Initial Offering Price Per Share		$
Historical Net Tangible Book Value Per Share as of December 30, 2016	$ (0.84)	
Increase in Net Tangible Book Value Per Share Attributable to New Investors		
As Adjusted Net Tangible Book Value Per Share After this Offering		
Dilution Per Share to New Investors		

If the underwriters exercise the option to purchase an additional $ million of shares of our common stock in full, the as adjusted net tangible book value per share, after giving effect to the offering, would be $ per share. This represents an immediate increase in as adjusted net tangible book value of $ per share to existing stockholders and an immediate dilution in as adjusted net tangible book value of $ per share to new investors purchasing common stock in this offering. Moreover, if any additional shares are issued in connection with outstanding options or warrants, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our stockholders.

Each $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase our net tangible book value after this offering by approximately $ million, or approximately $ per share, and the dilution per share to new investors by approximately $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, an increase (decrease) of one million shares in the number of shares offered by us would increase our net tangible book value after this offering by approximately $ million, or $ per share, and decrease the dilution per share to new investors by approximately $ per share, assuming that the assumed public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The number of shares of our common stock to be outstanding after this offering is based on 10,023,810 shares of our common stock outstanding as of December 31, 2016, and excludes the following:

- 2,000,000 shares of our common stock reserved for issuance under our 2015 Incentive Plan (there have been no options granted or other securities issued under our 2015 Incentive Plan);
- shares of our common stock convertible upon the completion of our initial public offering related to the sale of convertible notes in December 2016 in the aggregate amount of $200,000; and
- shares underlying a warrant to be issued to National Securities Corporation following our initial public offering.

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

Forward-Looking Statements

Statements in the following discussion and throughout this registration statement that are not historical in nature are "forward-looking statements." You can identify forward-looking statements by the use of words such as "expect," "anticipate," "estimate," "may," "will," "should," "intend," "believe," and similar expressions. Although we believe the expectations reflected in these forward-looking statements are reasonable, such statements are inherently subject to risk and we can give no assurances that our expectations will prove to be correct. Actual results could differ from those described in this registration statement because of numerous factors, many of which are beyond our control. These factors include, without limitation, those described under Item 1A "Risk Factors." We undertake no obligation to update these forward-looking statements to reflect events or circumstances after the date of this registration statement or to reflect actual outcomes. Please see "Forward Looking Statements" at the beginning of this registration statement.

The following discussion of our financial condition and results of operations should be read in conjunction with our financial statements and the related notes thereto and other financial information appearing elsewhere in this registration statement. We undertake no obligation to update any forward looking statements in the discussion of our financial condition and results of operations to reflect events or circumstances after the date of this registration statement or to reflect actual outcomes.

Overview

We are a specialty pharmaceutical company that acquires, licenses, develops and commercializes products principally for use in the acute/intensive care hospital setting. Our initial product candidate is IV Tramadol, for the management of moderate to moderately severe postoperative pain. In the first quarter of 2016, we completed a PK study for IV Tramadol in healthy volunteers and had an EOP2 meeting with the FDA. We plan to initiate a Phase 3 development program of IV Tramadol for the management of postoperative pain in 2017. Under the terms of certain agreements described herein, we have an exclusive license to develop and commercialize IV Tramadol in the United States. We plan to seek additional products to develop in the acute/intensive care hospital market in addition to IV Tramadol. To date, we have not received approval for the sale of our product candidate in any market and, therefore, have not generated any product sales from our product candidate.

We are a majority controlled subsidiary of Fortress.

Avenue Therapeutics, Inc. was incorporated in Delaware on February 9, 2015. Our executive offices are located at 2 Gansevoort Street, 9th Floor, New York, NY 10014. Our telephone number is (781) 652-4500, and our website is *www.avenuetx.com*.

Critical Accounting Policies and Use of Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued expenses and stock-based compensation. We base our estimates on historical experience, known trends and events and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our significant accounting policies are described in more detail in the notes to our financial statements included elsewhere in this prospectus.

Results of Operations

Comparison of Year Ended December 31, 2016 to Period Ended December 31, 2015 from February 9, 2015 (Inception)

General

At December 31, 2016, we had an accumulated deficit of $8.4 million, primarily as a result of expenditures for licenses acquired, research and development and general and administrative purposes. At December 31, 2015 (from inception), we had an accumulated deficit of $5.2 million, primarily as a result of expenditures for licenses acquired. While we may in the future generate revenue from a variety of sources, including license fees, milestone payments, research and development payments in connection with strategic partnerships and/or product sales, our product candidate is in early stages of development and may never be successfully developed or commercialized. Accordingly, we expect to continue to incur substantial losses from operations for the foreseeable future, and there can be no assurance that we will ever generate significant revenues.

Research and Development Expenses

Research and development expenses primarily consist of personnel related expenses, including salaries, benefits, travel, other related expenses, stock-based compensation, payments made to third parties for license and milestone costs related to in-licensed products and technology, payments made to third party contract research organizations for preclinical and clinical studies, investigative sites for clinical trials, consultants, the cost of acquiring and manufacturing clinical trial materials, costs associated with regulatory filings, laboratory costs and other supplies.

For the year ended December 31, 2016, and for the period from February 9, 2015 (inception) to December 31, 2015, research and development expenses were approximately $1.3 million and $1.0 million, respectively. For the year ended December 31, 2016, $0.9 million relates to the development of IV Tramadol, in particular the PK Study we conducted in the first half of 2016, $0.25 million relates to payments made pursuant to our Management Services Agreement with Fortress and $0.2 million for personnel costs. For the period from February 9, 2015 (inception) through December 31, 2015, $0.7 million relates to activities in connection with the development of IV Tramadol, $0.2 million relates to payments made pursuant to our Management Services Agreement with Fortress and $0.1 million for personnel costs.

For the year ended December 31, 2016, and for the period from February 9, 2015 (inception) to December 31, 2015, research and development-licenses acquired were $49,000 and $3.0 million, respectively. The $49,000 represents payment of the annual Class A Preferred Stock dividend and the $3.0 million is comprised of the upfront payment for the IV Tramadol license we acquired in 2015 and $40,000 for the 2.5% equity fee paid pursuant to the Founders' Agreement. In 2016, this annual equity fee was replaced with the Class A Preferred Stock dividend.

We expect our research and development activities to increase as we develop our existing product candidate and potentially acquire new product candidates, reflecting increasing costs associated with the following:

- employee-related expenses, which include salaries and benefits, and rent expenses;
- license fees and milestone payments related to in-licensed products and technology;
- expenses incurred under agreements with contract research organizations, investigative sites and consultants that conduct our clinical trials and a substantial portion of our preclinical activities;
- the cost of acquiring and manufacturing clinical trial materials; and
- costs associated with non-clinical activities, and regulatory approvals.

General and Administrative Expenses

General and administrative expenses consist principally of professional fees for legal and consulting services, personnel-related costs, and other general operating expenses not otherwise included in research and development expenses.

For the year ended December 31, 2016, and for the period from February 9, 2015 (inception) to December 31, 2015, general and administrative expenses were approximately $1.0 million and $0.8 million, respectively. For the year ended December 31, 2016, $0.25 million relates to payments made pursuant to our Management Services Agreement with Fortress, $0.6 million relates to professional fees and $0.2 million relates personnel costs. For the period from February 9, 2015 (inception) through December 31, 2015, $0.6 million was for professional fees in connection with the acquisition of the license from Revogenex as well as formation costs, $0.2 million related to payments pursuant to the Management Services Agreement with Fortress, and approximately $0.1 million related to personnel costs.

We anticipate that our general and administrative expenses will increase in future periods, reflecting continued and increasing costs associated with:

- support of our expanded research and development activities;
- stock compensation granted to key employees and non-employees;
- support of business development activities; and
- increased professional fees and other costs associated with the regulatory requirements and increased compliance associated with being a public reporting company.

Liquidity and Capital Resources

We have incurred substantial operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future and may never become profitable. As of December 31, 2016, we had an accumulated deficit of $8.4 million.

In February 2015, Fortress completed a private placement of a promissory note for $10 million through National Securities Corporation, or the NSC Note. National Securities Corporation, or NSC, a wholly owned subsidiary of National Holdings, Inc., acted as the sole placement agent for the NSC Note. Fortress used the proceeds from the NSC Note to acquire medical technologies, products and for activities related to the formation of its subsidiaries. The NSC Note matures 36 months after issuance, provided that during the first 24 months, Fortress can extend the maturity date by six months. No principal amount will be due for the first 24 months after issuance (or the first 30 months after issuance if the maturity date is extended). Thereafter, the NSC Note will be repaid at the rate of 1/12 of the principal amount per month for a period of 12 months. Interest on the NSC Note is 8%, payable quarterly during the first 24 months after issuance (or the first 30 months after issuance if the NSC Note is extended) and monthly during the last 12 months.

Fortress used some of the proceeds from the NSC Note to acquire our license agreement, by transferring part of this indebtedness to us. The NSC Note allows Fortress to transfer a portion of the indebtedness (and proceeds) from the NSC Note to us. On October 31, 2015, we executed an additional note (with the same terms as the NSC Note) for $3.0 million in favor of NSC, representing a transfer of indebtedness from Fortress to us. We have recorded interest expense of approximately $0.3 million and $0.2 million related to our $3 million note in interest expense (includes discount amortization) in our statements of operations for the year ended December 31, 2016, and for the period from February 9, 2015 (inception) to December 31, 2015, respectively.

In addition, in accordance with the terms of the NSC Note, on October 31, 2015 we issued a warrant to NSC equal to 25% of the amount of NSC Note proceeds we received from Fortress divided by the lowest price at which we next sold common stock. The warrant issued has a term of ten years and an exercise price equal to the par value of our common stock.

On January 3, 2017, in accordance with the terms of the NSC Note, Fortress notified NSC of its intention to extend the maturity date of the original note by six months to September 30, 2018.

Through December 31, 2016, we funded our operations through the NSC Note and an Intercompany Working Capital Promissory Note with Fortress, or the Fortress Note. As of December 31, 2016, approximately $2.8 million was outstanding under the Fortress Note. We have recorded interest expense of $0.2 million and $0.2 million related to the Fortress Note in interest expense in our statements of operations for the year ended December 31, 2016, and for the period from February 9, 2015 (inception) to December 31, 2015, respectively.

We will need to raise capital in order to proceed with the Phase 3 development program for IV Tramadol in 2017, which is estimated to cost approximately $30 million. Our plans to raise capital may not be successful. These factors, among others, raise substantial doubt about our ability to continue as a going concern.

In December 2016, we sold three convertible promissory notes to investors for an aggregate of $0.2 million. The notes have an initial term of 18 months, which can be extended at the option of the holder, on one or more occasions, for up to 180 days and accrue simple interest at the rate of 5% per annum for the first 12 months and 8% per annum simple interest thereafter. The notes are guaranteed by Fortress. The outstanding principal and interest of the notes automatically converts into the type of equity securities sold by us in the next sale of equity securities in which we realize aggregate gross cash proceeds of at least $10.0 million (before commissions or other expenses and excluding conversion of the notes) at a conversion price equal to the lesser of (a) the lowest price per share at which our equity securities are sold in such sale less a 33% discount and (b) a per share price based on a pre-offering valuation of $30.0 million divided by the number of common shares outstanding on a fully-diluted basis.

Upon the closing of these three promissory notes in December 2016, we realized net proceeds of $142,000 after paying WestPark Capital, Inc., the placement agent, placement agent fees of $30,000 and escrow fees of $4,000 and paying approximately $14,000 in legal fees. Additionally, WestPark Capital, Inc. received a warrant, or the WestPark Warrant, to purchase the number of shares of our common stock equal to $10,000 divided by the price per share at which any note sold to investors first converts into our common stock. The WestPark Warrant has a ten-year term and has a per share exercise price equal to the price per share at which any note sold to investors first converts into our common stock.

Recently Issued Accounting Pronouncements

In January 2017, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2017-04, *Intangibles — Goodwill and Other* (Topic 350): Simplifying the Test for Goodwill Impairment, or ASU 2017-04, which eliminates the second step of the previous FASB guidance for testing goodwill for impairment and is intended to reduce cost and complexity of goodwill impairment testing. The amendments in this ASU modify the concept of impairment from the condition that exists when the carrying amount of goodwill exceeds its implied fair value to the condition that exists when the carrying amount of a reporting unit exceeds its fair value. After determining if the carrying amount of a reporting unit exceeds its fair value, the entity should take an impairment charge of the same amount to the goodwill for that reporting unit, not to exceed the total goodwill amount for that reporting unit. This eliminates the second step of calculating the implied fair value of goodwill by assigning the fair value of a reporting unit to all of its assets and liabilities as if that reporting unit had been acquired in a business combination. ASU 2017-04 is effective for annual periods beginning after December 15, 2019, including interim periods within those annual periods. Early adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. We are currently evaluating the impact of adopting the new guidance on our financial statements.

In January 2017, FASB issued ASU 2017-01, "*Business Combinations (Topic 805) Clarifying the Definition of a Business*" The amendments in this update is to clarify the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The definition of a business affects many areas of accounting including acquisitions, disposals, goodwill, and consolidation. The guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. We are currently evaluating the impact of adopting this guidance.

In August 2016, the FASB issued ASU No. 2016-15,*Statement of Cash Flows — Classification of Certain Cash Receipts and Cash Payments*, which addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. We are currently in the process of evaluating the impact of this new pronouncement on our statements of cash flows.

In April 2016, the FASB issued ASU No. 2016-10,*Revenue from Contracts with Customer*, or ASU 2016-10. The new guidance is an update to ASC 606 and provides clarity on identifying performance obligations and licensing implementation. For public companies, ASU 2016-10 is effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2016. We are currently evaluating the impact that ASU 2016-10 will have on our financial statements.

In March 2016, the FASB issued ASU No. 2016-09*Compensation-Stock Compensation (Topic 718), Improvements to Employee Share-Based Payment Accounting*, or ASU 2016-09. Under ASU 2016-09, companies will no longer record excess tax benefits and certain tax deficiencies in additional paid-in capital, or APIC. Instead, they will record all excess tax benefits and tax deficiencies as income tax expense or benefit in the income statement and the APIC pools will be eliminated. In addition, ASU 2016-09 eliminates the requirement that excess tax benefits be realized before companies can recognize them. ASU 2016-09 also requires companies to present excess tax benefits as an operating activity on the statement of cash flows rather than as a financing activity. Furthermore, ASU 2016-09 will increase the amount an employer can withhold to cover income taxes on awards and still qualify for the exception to liability classification for shares used to satisfy the employer's statutory income tax withholding obligation. An employer with a statutory income tax withholding obligation will now be allowed to withhold shares with a fair value up to the amount of taxes owed using the maximum statutory tax rate in the employee's applicable jurisdiction(s). ASU 2016-09 requires a company to classify the cash paid to a tax authority when shares are withheld to satisfy its statutory income tax withholding obligation as a financing activity on the statement of cash flows. Under current GAAP, it was not specified how these cash flows should be classified. In addition, companies will now have to elect whether to account for forfeitures on share-based payments by (1) recognizing forfeitures of awards as they occur or (2) estimating the number of awards expected to be forfeited and adjusting the estimate when it is likely to change, as is currently required. The amendments of this ASU are effective for reporting periods beginning after December 15, 2016, with early adoption permitted but all of the guidance must be adopted in the same period. We are currently assessing the impact the adoption of ASU 2016-09 will have on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02,*Leases (Topic 842)*, or ASU 2016-02, which supersedes FASB Accounting Standards Codification, or ASC, Topic 840, *Leases (Topic 840)* and provides principles for the recognition, measurement, presentation and disclosure of leases for both lessees and lessors. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease

liability for all leases with a term of greater than twelve months regardless of classification. Leases with a term of twelve months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for annual and interim periods beginning after December 15, 2018, with early adoption permitted upon issuance. We are currently evaluating the method of adoption and the impact of adopting ASU 2016-02 on our financial statements. When adopted, we do not expect this guidance to have a material impact on our financial statements.

In January 2016, the FASB issued ASU No. 2016-01,*Recognition and Measurement of Financial Assets and Financial Liabilities*, or ASU 2016-01. ASU 2016-01 requires equity investments to be measured at fair value with changes in fair value recognized in net income; simplifies the impairment assessment of equity investments without readily determinable fair values by requiring a qualitative assessment to identify impairment; eliminates the requirement for public business entities to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet; requires public business entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes; requires an entity to present separately in other comprehensive income the portion of the total change in the fair value of a liability resulting from a change in the instrument-specific credit risk when the entity has elected to measure the liability at fair value in accordance with the fair value option for financial instruments; requires separate presentation of financial assets and financial liabilities by measurement category and form of financial assets on the balance sheet or the accompanying notes to the financial statements and clarifies that an entity should evaluate the need for a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the entity's other deferred tax assets. ASU 2016-01 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. We are currently evaluating the impact that ASU 2016-01 will have on our balance sheet or financial statement disclosures. When adopted, we do not expect this guidance to have a material impact on our financial statements.

In November 2015, the FASB issued ASU No. 2015-17,*Balance Sheet Classification of Deferred Taxes*, or ASU 2015-17. ASU 2015-17 requires that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. ASU 2015-17 is effective for financial statements issued for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. We are currently evaluating the impact that ASU 2015-17 will have on our balance sheet or financial statement disclosures. When adopted, we do not expect this guidance to have a material impact on our financial statements.

In April 2015, the FASB issued ASU No. 2015-03,*Simplifying the Presentation of Debt Issuance Costs*, or ASU 2015-03, which requires debt issuance costs to be presented in the balance sheet as a direct deduction from the carrying value of the associated debt liability, consistent with the presentation of a debt discount. ASU 2015-03 is effective for the interim and annual periods ending after December 15, 2015, with early adoption permitted. We adopted ASU 2015-03 and such adoption resulted in debt issuance costs presented as an offset against notes payable, long-term, in the accompanying balance sheet.

In August 2014, the FASB issued ASU No. 2014-15,*Presentation of Financial Statements-Going Concern*, or ASU 2014-15, which defines management's responsibility to assess an entity's ability to continue as a going concern, and to provide related footnote disclosures if there is substantial doubt about its ability to continue as a going concern. ASU 2014-15 is effective for annual reporting periods ending after December 15, 2016, with early adoption permitted. We adopted ASU 2014-15 in the fourth quarter of 2016, and its adoption did not have a material impact on our financial statements.

Contractual Obligations and Commitments

The following table reflects a summary of our estimates of future material contractual obligations as of December 31, 2016. Future events could cause actual payments to differ from these estimates.

	Total	Less than 1 year	1 – 3 years	3 – 5 years	More than 5 years
Contractual obligations:					
NSC notes	$ 3,000,000	$ 1,000,000	2,000,000	—	—
Convertible notes	200,000	—	200,000	—	—
License acquired	4,000,000	—	1,000,000	3,000,000	—
Total contractual obligations	$ 7,200,000	$ 1,000,000	3,200,000	3,000,000	—

As of December 31, 2016, we have $7.2 million in contracted obligations, consisting of a $3.0 million note to NSC, $0.2 million of convertible notes and $4.0 million of milestone payments due to Revogenex in connection with the achievement of certain development milestones.

Qualitative and Quantitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. We had cash and cash equivalents of $14,000 as of December 31, 2015 and $0.2 million as of December 31, 2016, consisting of cash and money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

Off-Balance Sheet Arrangements

We are not party to any off-balance sheet transactions. We have no guarantees or obligations other than those which arise out of normal business operations.

BUSINESS

Overview

We are a specialty pharmaceutical company focused on the development and commercialization of an intravenous, or IV, formulation of tramadol HCl, or IV Tramadol, for the management of moderate to moderately severe postoperative pain. Tramadol is a synthetic dual-acting opioid with a well-established efficacy and safety profile, and has been used throughout the world for more than 30 years, accumulating an abundance of available clinical data. Oral tramadol is currently approved and marketed in the United States for moderate to moderately severe pain in adults, and physicians are already familiar with the oral dosage of the drug. Parenteral tramadol is approved and used for the management of moderate to moderately severe postoperative pain throughout much of the world, but there is no parenteral formulation currently available in the United States. We anticipate that the introduction of an intravenous formulation in the United States will address the current market need presented by the shortcomings of opioids and other analgesics currently used in the postoperative setting. We have an exclusive license to develop and commercialize IV Tramadol in the United States and we also plan to seek additional products to develop in the acute/intensive care hospital market in addition to IV Tramadol.

In 2016, we completed a pharmacokinetics, or PK, study for IV Tramadol in healthy volunteers as well as an End-of-Phase 2, or EOP2, meeting with the U.S. Food and Drug Administration, or the FDA. We plan to initiate a Phase 3 development program of IV Tramadol for the management of postoperative pain in 2017. We intend to conduct two pivotal Phase 3 trials for IV Tramadol. We plan to initiate the first Phase 3 trial in patients with moderate-to-severe pain following bunionectomy in the third quarter of 2017. We anticipate that we will have topline data as early as the second quarter of 2018. We plan to initiate the second Phase 3 trial in patients with moderate-to-severe pain following abdominoplasty in the third quarter of 2018, upon successful completion of the bunionectomy study. Based on the enrollment pace of similar studies, we anticipate that we will have topline data from this second Phase 3 trial as early as mid-2019. We also plan to conduct an open-label safety study, which will run concurrently with the two Phase 3 trials. If these studies are successful, we plan to submit a new drug application, or an NDA, for IV Tramadol to treat moderate to moderately severe postoperative pain pursuant to Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, or the FDCA, by the end of 2019.

Our Strategy

Our primary objective is to establish IV Tramadol as an invaluable part of a treating physician's repertoire of available pharmaceutical options for the management of postoperative pain. The key elements of our strategy include:

- *Complete our Phase 3 program for IV Tramadol.* We expect to commence our Phase 3 program in the third quarter of 2017 and expect to report topline data from our two pivotal trials as early as the second quarter of 2018 and mid-2019, respectively. We also plan to conduct an open-label safety study, which will run concurrently with the two Phase 3 trials.
- *Obtain FDA approval of IV Tramadol for the management of moderate to moderately severe postoperative pain.* If our Phase 3 trials meet their primary endpoints, we plan to submit our NDA for IV Tramadol by the end of 2019. We intend to seek FDA approval of IV Tramadol pursuant to Section 505(b)(2) of the FDCA.
- *Commercially launch IV Tramadol in the United States.* We intend to directly commercialize IV Tramadol in the United States, if approved, using a small hospital-based sales force. Alternatively, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidate.

- *Maintain, expand and protect our intellectual property portfolio.* We intend to expand and protect our intellectual property in the area of IV administration of tramadol in order to maintain a defensible and valuable intellectual property portfolio.
- *Expand our product portfolio through acquiring or in-licensing additional late-stage, or new versions of currently approved hospital-focused products.* We will seek additional opportunities to acquire or in-license products to more fully utilize our clinical, regulatory, manufacturing, sales and marketing capabilities. To reduce the time-to-market and the risks and costs of clinical development, we are focusing on products that are in late-stages of development, currently commercialized outside the United States or approved in the United States but with significant commercial potential for proprietary new uses or formulations.
- *Pursue additional indications and commercial opportunities for our product candidates.* We will seek to maximize the value of IV Tramadol and any other product candidates we may in-license, acquire or develop by pursuing other indications and commercial opportunities for such candidates.

The U.S. Postoperative Pain Market

We are currently focused on developing our proprietary product candidate, IV Tramadol, for the management of moderate to moderately severe postoperative pain. Even though the postoperative pain market is entrenched with low cost, generic pain relievers, we believe that there still remains a significant unmet medical need for safer and better-tolerated painkillers, which are also referred to as analgesics.

According to Decision Resources' Acute Pain Report of October 2014, or the 2014 Pain Report, sales of analgesics delivered via parenteral routes (IV, subcutaneous, and intramuscular injections) for the management of acute pain totaled approximately $965 million in the United States in 2013. According to the 2014 Pain Report, there were over ten million select common inpatient procedures performed, all of which likely required postoperative pain management, in the United States in 2013. According to IMS Health, injectable analgesics sold approximately $1 billion in the United States in 2015.

The major goal in the management of postoperative pain is minimizing the dose of medications to lessen side effects while still providing adequate pain relief for analgesia. This is best accomplished with multimodal and preemptive analgesia. An effective pain relief program should be individualized for the particular patient, operation, and circumstances. In clinical practice, as there is no standard set of guidelines to manage postoperative pain, hospitals and even hospital units have their own practice guidelines that are often based on physicians' prescribing practices. These local guidelines are rooted in physician experience as it relates to anticipated severity of pain due to a particular surgical procedure, and are often modified with consideration to things like staffing limitations, availability of specific drugs and/or formulations, access to patient controlled analgesia, or PCA, systems, and formulary restrictions. Thus, treatment regimens vary widely from hospital to hospital, physician to physician and patient to patient.

Understanding the range of available interventions and considering the type of surgery is essential to safe and effective pain management. The general consensus among pain management practitioners is that use of more than one modality (i.e., molecules with different mechanisms or with different routes of administration) is optimal for successful postoperative pain management. The most commonly prescribed agents in the immediate postoperative pain market are typically acetaminophen, or APAP, NSAIDS, and opioid analgesics. APAP and NSAIDs are not sufficiently effective as the sole agent for pain management after major surgery in most patients. However, when used in conjunction with opioids, APAP and NSAIDs offer substantial benefits as the quality of analgesia is often improved or enhanced due to their differentiated mechanism of action. Nevertheless, the substantial side effects associated with these agents represent an important concern for patients and physicians to address. NSAIDS in particular have their own serious side

effects, including increased post-surgery bleeding, peptic ulcer disease and renal impairment, and is associated with hepatic side effects.

Traditional opioids offer safe and effective postoperative pain control and can be used in combination with other agents and techniques. However, the side effects of opioids, such as morphine, include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression. Physical dependence and addiction are clinical concerns that may prevent proper prescribing and, in turn, inadequate pain management. Less common side effects include delayed gastric emptying, hyperalgesia, immunologic and hormonal dysfunction, muscle rigidity, and myoclonus.

Therefore, there is still unmet medical need in the post-surgical setting. We believe that IV Tramadol can fill this unmet need. If approved for its intended indication, we believe that IV Tramadol will be an opioid effective in treating moderate to moderately severe pain without the side effects often seen with traditional opioids.

The table below summarizes the available intravenous analgesic options in postoperative pain management currently available in the United States.

Available Classes	Pain Levels	Common Limitations & Contraindications
IV narcotics	Moderate to severe	Strong sedation Respiratory depression Constipation Risk of dependence
IV NSAIDS	Mild to moderately severe	Post-op bleeding risk GI side effects Renal impairment
IV acetaminophen	Mild to moderate	Hepatic impairment

Our Product Candidate

Tramadol, a synthetic dual-acting opioid, is a centrally acting analgesic with weak opioid agonist properties. It also works via the inhibition of serotonin and noradrenaline re-uptake and blocking nociceptive impulses at the spinal level. These opioid and non-opioid modes of action are synergistic, essentially providing “multimodal therapy” with the use of a single drug. Tramadol is also commonly combined with APAP or NSAIDS in clinical practice. Tramadol has a well-established efficacy and safety profile and has been used throughout the world for more than 30 years. In the United States, tramadol is approved and marketed as an oral agent for moderate to moderately severe pain in adults. Tramadol was first approved in the United States in 1995, under the trade name Ultram® immediate release tablet, and is available as 50 mg, 100 mg, and 200 mg dosage forms (Ortho-McNeil-Janssen). Ultracet®, a combination product containing tramadol and acetaminophen, is also marketed in the United States (Ortho-McNeil-Janssen). According to Symphony Health Solutions, over 40 million scripts for tramadol and tramadol-containing drugs have been prescribed annually in the United States since 2012.

Tramadol use is associated with fewer side effects compared with the use of other opioids for pain management. Tramadol causes less respiratory depression, has minimal effect on the body’s hemodynamic function, and does not impair immune function. Tramadol also causes minimal gastrointestinal adverse effects, including reduced constipation compared to other opioids. The most common side effects are nausea and dizziness. Importantly, tramadol has low potential for abuse and addiction and is currently classified by the DEA as a Schedule IV controlled substance. For comparison, other opioids which have a high potential for abuse, including meperidine, morphine, hydromorphone and oxycodone, are all classified as Schedule II controlled substances.

Oral tramadol was generally well tolerated in clinical trials evaluating its analgesic safety and efficacy. It has demonstrated utility in patients with a risk of poor cardiopulmonary function, after surgery of the thorax or upper abdomen and when non-opioid analgesics are contraindicated.

The efficacy of oral and parenteral tramadol in relieving moderate to moderately severe postoperative pain associated with surgery was demonstrated in several comparative human clinical trials.

The clinical trials summarized below show that the overall analgesic efficacy of parenteral tramadol was similar to that of morphine and meperidine and comparable or superior to that of pentazocine:

- In a clinical trial published in *Drugs under Experimental and Clinical Research* (*http://www.ncbi.nlm.nih.gov/pubmed/9604144*), 70 patients were treated with parenteral morphine or tramadol following abdominal surgery. Both drugs gave rapid and constant pain relief. The study investigators concluded that tramadol given by intramuscular injection has postoperative analgesic activity similar to morphine, and was better tolerated.
- In a clinical trial published in *Methods and Findings in Experimental and Clinical Pharmacology* (*http://www.ncbi.nlm.nih.gov/pubmed/8738073*), 48 patients after total hip or knee replacement were randomly distributed into three groups and received tramadol, meperidine or saline in a double-blind manner. The conclusion of the study was that meperidine and tramadol produced comparable analgesia, but meperidine induced sedation and respiratory depression while tramadol did not.
- In a clinical trial published in *International Journal of Pharmacological Research* (*http://www.ncbi.nlm.nih.gov/pubmed/9675626*), a total of 50 adults were given tramadol or pentazocine by intramuscular injection for three days post-surgery. The first dose of tramadol was significantly more effective than pentazocine after the first hour. Study investigators concluded that final judgements on efficacy and acceptability were in favor of tramadol while both produced good analgesia.

Advantages of IV Tramadol

Parenteral tramadol is approved and used for the management of moderate to moderately severe postoperative pain throughout much of the world. Parenteral formulations include IV, intramuscular, or IM, and subcutaneous, or SC, formulations. Based on our review of IMS Health data from 2014 to 2016, we believe that parenteral tramadol accounts for approximately 10% of the total IV analgesics used in Europe. There is no parenteral formulation currently approved in the United States.

We believe that the introduction of an IV formulation of tramadol in the United States will address many of the shortcomings of opioids, APAP and NSAIDs currently used in the postoperative setting.

We plan to administer IV Tramadol over approximately 15 minutes in our Phase 3 trials. We believe that our method of administration of IV Tramadol may provide significant benefits such as reduced side effects, compared to previously approved methods of administration of IV Tramadol in Europe, which is typically accomplished via a slow push over 2 to 3 minutes. In addition, we believe our IV Tramadol dosing regimen produces a similar Cmax (maximal blood level) and AUC (overall systemic exposure) to those of oral tramadol at steady state, which ensures an easy transition from IV to oral therapy in the post-surgical setting.

Based on the trials done in Europe and on the data generated with oral tramadol, we believe that IV Tramadol, if approved, will be an attractive option for physicians who treat postoperative pain, due to the following attributes:

- As an established analgesic, tramadol has documented efficacy and safety for moderate to moderately severe pain and physicians are already familiar with the drug.
- As a Schedule IV controlled substance, tramadol has less potential for addiction and abuse than other narcotics widely prescribed in the post-surgical setting. In the current

environment where the opioid epidemic is a recognized problem in the United States and there are increasing restrictions on Schedule II opioids, a Schedule IV opioid such as tramadol may become a more attractive option.

- Tramadol's differentiated safety profile could make it an attractive alternative to currently available stand-of-care opioids. In particular, IV Tramadol could be a suitable choice for patients at risk for respiratory depression, elderly patients with cardiopulmonary compromise, patients with sleep apnea or contraindication to NSAIDS or those with a history of drug dependence or cannot tolerate traditional opioids.
- Importantly, there is a step-down therapy available for IV Tramadol. Patients are transitioned to oral therapy when they are discharged from the hospital or when they can tolerate oral medicine. Our IV Tramadol dosing regimen provides a similar PK profile to that of oral tramadol at steady state to ensure a smooth step-down process.

We believe that IV Tramadol will be a useful and effective tool in the management of acute postoperative pain. Its advantages compared to current standard-of-care agents, along with the known efficacy, safety and tolerability profile for tramadol support the use of IV Tramadol in this setting. We believe that the risks associated with the use of IV Tramadol will be benign compared to other opioids, and consistent with that of the currently marketed oral tramadol products. Consequently, with the industry trend toward multimodal therapy and away from Schedule II narcotics, we believe IV Tramadol's unique profile could position it to become an invaluable part of a treating physician's repertoire of available pharmaceutical options in the management of postoperative pain.

In 2016 we conducted a survey of 30 U.S. anesthesiologists regarding their impression of IV Tramadol. We believe that the feedback was favorable with the majority of physicians believing that IV Tramadol represents an improvement from currently available IV analgesics, and would be better tolerated than IV morphine and have similar or better efficacy than morphine. The table below summarizes the responses from the doctors in this survey.

Overall Impression	
Favorable initial impression of tramadol as a potential new IV analgesic	77%
Believes that IV tramadol is an improvement over current post-op pain meds	97%
Believes that IV tramadol is better than morphine on safety	87%
Believes that IV tramadol is similar or better than morphine on efficacy	67%

Patients taking	**Switch to IV tramadol**	**Add IV tramadol**
IV morphine	40%	41%
IV NSAIDS	26%	37%
IV acetaminophen	24%	35%

Clinical Development History

Revogenex completed multiple nonclinical PK and toxicology studies in dogs, a Phase 1 dose proportionality study and a thorough QT/QTc (TQT) study of IV Tramadol in healthy volunteers, or the TQT Study. The dose proportionality study was designed to compare maximum exposure and cumulative exposures of IV Tramadol to that of oral tramadol, and to assess the dose proportionality of IV Tramadol in healthy adult volunteers. The TQT Study was done to evaluate whether IV Tramadol has the potential to affect the "corrected QT interval", or QTc, in healthy volunteers. The QTc represents electrical depolarization and repolarization of the heart ventricles. A lengthened QTc is a marker for the potential of ventricular arrhythmias. The results of these studies are consistent with tramadol's known toxicology profile, pharmacokinetics and pharmacology.

PK Study for IV Tramadol

In general, Phase 2 clinical trials include initial proof-of-concept efficacy studies, dose-finding studies, and initial safety assessments in the target (i.e., to-be-treated) population. We did not conduct Phase 2 clinical trials for IV Tramadol because tramadol is a known analgesic, and oral tramadol is labeled for "moderate to moderately severe pain" in the United States. Instead, we completed pharmacokinetic simulations and conducted a pharmacokinetic and safety study in healthy volunteers, in order to select a Phase 3 dose and dosing regimen designed to achieve exposure to tramadol similar to that provided by oral tramadol. In 2016, we completed a PK study for IV Tramadol in healthy volunteers. A PK study generally involves dosing an experimental medicine in healthy volunteers and taking a series of blood measurements from the study participants to understand how the body handles the drug. A PK study provides information on important parameters such as systemic exposure, maximal and minimal levels of drug concentration in the blood and their time courses. The PK study we conducted was used to select a dose and dosing regimen of IV Tramadol that achieves similar exposure to that provided by oral tramadol at steady state.

The PK study was designed as a three-way cross over study in 18 healthy volunteers. Each subject in the study served as his/her own control and received oral tramadol as well as two different doses of IV Tramadol. Based on the results of the PK study, we have decided to use a 50 mg dose in our pivotal Phase 3 program. The specifics of the dosing regimen have not been disclosed, as they are the subject of a new patent application.

Our Clinical Development Strategy for IV Tramadol

At our EOP2 meeting with FDA, we discussed Phase 3 program requirements for IV Tramadol and confirmed the key elements of the Phase 3 program design. We plan to conduct two pivotal Phase 3 trials to evaluate the safety and efficacy of IV Tramadol, and one additional safety study. All three trials will enroll patients who require IV analgesia following surgery. We anticipate that approximately 1,000 patients will be enrolled in the total Phase 3 program. We believe that the design of our Phase 3 program is consistent with the design of Phase 3 programs for other analgesics being developed by Trevena, Inc., Cara Therapeutics, Inc., and Recro Pharma, Inc.

Postoperative pain following bunionectomy (orthopedic surgery model). The first Phase 3 trial will be conducted in patients undergoing bunionectomy surgery, which is considered an orthopedic surgical model. Approximately 405 patients will be randomized 1:1:1 to one of two doses of IV Tramadol, or placebo, for 48 hours. The primary efficacy endpoint is Sum of Pain Intensity Difference over 48 hours (SPID 48), which is a measure of the overall effectiveness of the drug in reducing pain intensity during the 48-hour period. We plan to initiate this trial in the third quarter of 2017. Based on the enrollment pace of similar clinical trials, we anticipate that we may have topline data as early as the second quarter of 2018.

Postoperative pain following abdominoplasty (soft tissue model). The second Phase 3 safety and efficacy trial will be conducted in patients undergoing abdominoplasty surgery, which is considered a soft-tissue surgical model. Approximately 360 patients will be randomized 3:3:2 to IV Tramadol, placebo or a standard-of-care comparator arm. The primary efficacy endpoint is Sum of Pain Intensity Difference over 24 hours (SPID 24). We plan to initiate this trial in the third quarter of 2018 upon the completion of the bunionectomy study. Based on the enrollment pace of similar trials, we anticipate that we may have topline data to be reported as early as mid-2019.

Open-label safety study. We plan to initiate the safety study in the second half of 2017, and will run this study concurrently with the two Phase 3 trials. Approximately 250 patients will be enrolled in the safety study, which has an open label, single arm design. We anticipate that we will complete this study as early as mid-2019.

If these trials are successful, we plan to submit an NDA for the FDA's review and approval for IV Tramadol to treat moderate to moderately severe postoperative pain pursuant to Section 505(b)(2) of the FDCA by the end of 2019.

License Agreement with Revogenex Ireland Ltd.

Effective as of February 17, 2015, Fortress obtained a worldwide (with the exception of Central America and South America with respect to 50 mg and 100 mg IV Tramadol HCl injections) exclusive license to make, market and sell IV Tramadol pursuant to an agreement with Revogenex, a privately held company in Dublin, Ireland, or the License Agreement. Under the terms of the License Agreement, Fortress paid Revogenex an up-front licensing fee of $2.0 million upon execution and an additional $1.0 million on June 17, 2015; two additional milestones totaling $4.0 million are due upon the completion of certain development goals. Additional high single-digit to low double-digit royalty payments on net sales of licensed products are due. Royalties will be paid on a product-by-product and country-by-country basis until the expiration in each country of the valid patent claim. In return, Fortress obtained the exclusive worldwide rights to U.S. Patent No. 8,895,622 "Intravenous Administration of Tramadol" issued on November 25, 2014, or the '622 Patent, U.S. Patent No. 9,561,195 issued on February 7, 2017, or the '195 Patent, and U.S. Patent No. 9,566,253 issued on February 14, 2017, or the '253 Patent (with the exception of Central America and South America with respect to 50 mg and 100 mg IV Tramadol HCl injections). Additionally, Fortress acquired the rights to an open U.S. Investigational New Drug Application pertaining to IV Tramadol, as well as all supporting documentation and relevant correspondence with the FDA. Further, under the License Agreement, Fortress assumed the rights and obligations of Revogenex under its current manufacturing agreement with Z.F. Polpharma S.A, or the Manufacturing Agreement. Fortress transferred all its rights and obligations under the License Agreement and the Manufacturing Agreement to us pursuant to an Asset Transfer Agreement, dated as of May 13, 2015.

The License Agreement will terminate on a product-by-product and country-by-country basis upon the expiration of the last licensed patent right, unless the agreement is earlier terminated. In addition to standard early termination provisions, the License Agreement may also be terminated early by: (i) Revogenex if the NDA has not been filed by August 17, 2019, and we have failed to use commercially reasonable efforts to carry out all of the product development, (ii) Revogenex if the FDA does not issue an approval or otherwise issues a "not approvable" notice for the NDA within 15 months after the NDA has been filed with the FDA, although this termination right will be tolled if we are using commercial reasonable efforts in our negotiations with the FDA for approval and if we receive a "not approvable" notice, we will have a 15 month period to correct any issues and re-submit the NDA for approval, (iii) us if we reasonably determine prior to NDA approval that the development of IV Tramadol is not economically viable, or (iv) either Revogenex or us (provided we are using or have used commercially reasonable efforts to commercialize IV Tramadol) if, after the third anniversary date of the commercial launch, we fail to achieve annual net sales with respect to IV Tramadol of at least $20 million in any given calendar year, with certain exceptions.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis of proprietary products. We face competition and potential competition from a number of sources, including pharmaceutical and biotechnology companies, generic drug companies, drug delivery companies and academic and research institutions. In addition, companies that are active in different but related fields represent substantial competition for us. Many of our competitors have significantly greater capital resources, larger research and development staffs and facilities and greater experience in drug development, regulation, manufacturing and marketing than we do. These organizations also compete with us to recruit qualified personnel, attract partners for joint ventures or other collaborations, and license technologies that are competitive with ours. To compete successfully in this industry we must identify novel and unique drugs or methods of treatment and then complete the development of those drugs as treatments before our competitors do so.

We believe that IV Tramadol will compete with a number of opioid and non-opioid drugs that are currently available for the management of acute pain or in development. The most commonly used opioids in the postoperative and acute pain settings are morphine, hydromorphone and fentanyl. The non-opioid drugs used in this setting include Ofirmev (IV acetaminophen) and IV formulations of NSAIDs such as Dyloject (diclofenac), Toradol (ketorolac), and Caldolor (ibuprofen). In addition, we also expect to compete with agents such as Exparel, a liposome injection of bupivacaine indicated for administration into the surgical site to produce postsurgical analgesia.

In addition to approved products, there are a number of product candidates in development for the management of acute pain. The late-stage pain development pipeline is replete with reformulations and fixed-dose combination products of already available therapies. Among specific drug classes, opioid analgesics and NSAIDs represent the greatest number of agents in development. Most investigational opioids that have reached the later stages of clinical development are new formulations of already marketed opioids. Likewise, investigational NSAIDs — mostly lower dose injectable reformulations of already approved compounds — are another significant area of late-stage drug development in the postoperative pain space. There are also several agents with novel mechanisms in clinical development, such as CR845 (Cara Therapeutics, Inc.) and TRV130 (Trevena, Inc.).

Intellectual Property and Patents

General

Our goal is to obtain, maintain and enforce patent protection for our proprietary technologies, including methods of treatment, to preserve our trade secrets, and to operate without infringing on the proprietary rights of other parties, both in the United States and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents in the United States.

Patents and other proprietary rights are crucial to the development of our business. We will be able to protect our proprietary technologies from unauthorized use by third parties only to the extent that our proprietary rights are covered by valid and enforceable patents, supported by regulatory exclusivity or are effectively maintained as trade secrets. We have several patents and patent applications related to our proprietary technology, but we cannot guarantee the scope of protection of the issued patents, or that such patents will survive a validity or enforceability challenge, or that any of the pending patent applications will issue as patents.

Generally, patent applications in the United States are maintained in secrecy for a period of 18 months or more. The patent positions of biotechnology and pharmaceutical companies are highly uncertain and involve complex legal and factual questions. Therefore, we cannot predict the breadth of claims allowed in biotechnology and pharmaceutical patents, or their enforceability. To date, there has been no consistent policy regarding the breadth of claims allowed in biotechnology patents. Third parties or competitors may challenge or circumvent our patents or patent applications, if issued. If our competitors prepare and file patent applications in the United States that claim technology also claimed by us, we may have to participate in interference proceedings declared by the USPTO to determine priority of invention, which could result in substantial cost, even if the eventual outcome is favorable to us. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before we commercialize any of our products, any related patent may expire or remain in existence for only a short period following commercialization, thus reducing any advantage of the patent. However, the life of a patent covering a product that has been subject to regulatory approval may have the ability be extended through the patent restoration program, although any such extension could still be minimal.

If a patent is issued to a third party containing one or more preclusive or conflicting claims, and those claims are ultimately determined to be valid and enforceable, we may be required to obtain a license under such patent or to develop or obtain alternative technology, neither of which may be possible. In the event of litigation involving a third party claim, an adverse outcome in the litigation could subject us to significant liabilities to such third party, require us to seek a license for the disputed rights from such third party, and/or require us to cease use of the technology. Moreover, our breach of an existing license or failure to obtain a license to technology required to commercialize our products may seriously harm our business. We also may need to commence litigation to enforce any patents issued to us or to determine the scope and validity of third party proprietary rights. Litigation would involve substantial costs.

IV Tramadol

Pursuant to the License Agreement described below, we have exclusive, worldwide commercialization rights to the '622 Patent. The '622 Patent is directed to and claims methods of: treating pain by administering a therapeutically effective dose of tramadol intravenously over a time period from 10 minutes to about 45 minutes (i.e., the rate of IV Tramadol administration); administration over that time period for treating pain in humans by intravenously administering tramadol in solution at a range of concentrations; a method for treating acute pain in humans by administering IV Tramadol over 10 to 30 minutes; a method of treating acute postoperative pain by administering tramadol to a human patient intra-operatively at wound closure, or from first demand of analgesia postoperatively intravenously over a time period from 10 to 30 minutes; administering further doses of IV Tramadol at two to six hour time intervals for at least 48 hours post-surgery and administering an intravenous opioid analgesic which is not tramadol to the patient to further treat the patient's pain. Further claims of the '622 patent are directed to the 50 mg tramadol dose. These methods of treatment may provide significant benefits (e.g., reduced side effects) over previously approved methods of administration of IV Tramadol, in which the dose was typically accomplished over a two to three minute period. Additional claims of the '622 Patent focus on the intravenous administration of tramadol over 15 (±2) minutes, which represents the preferred method of administration that we will be pursuing in obtaining approval of our product through the FDA. The '622 Patent further describes and claims pharmacokinetic properties of our proprietary method of treatment (e.g., Tmax, Cmax and AUC), which are different from the previously achieved pharmacokinetics of prior IV Tramadol formulations, such as Tramal® solution for injection (available outside the U.S.). This patent is scheduled to expire on April 12, 2032 (absent possible patent term extensions).

In view of additional prior art discovered after the issuance of the '622 Patent, we have focused efforts on obtaining further patent coverage for the technology. Pursuant to the License Agreement, we have exclusive, worldwide commercialization rights to two all continuation patent filings of the '622 Patent. As a first step, we have prosecuted further claims in two continuation patent applications of the '622 patent in which all prior art which we were uncovered in extensive searches was brought to the attention of the USPTO. The goal was to obtain further patent claims which patentably differentiate over such prior art. To date, our efforts have resulted in the issuance of U.S. Patent No. 9,561,195 (hereinafter referred to as "the '195 Patent" which was issued from U.S. Application Serial No. 14/550,279 on February 7, 2017) and U.S. Patent 9,566,253 (hereinafter referred to as "the '253 Patent" which was issued from U.S. Application Serial No. 14/713,775 on February 14, 2017), both of which are entitled "Intravenous Administration of Tramadol" and both of which contain the same disclosure (specification) as that of the '622 Patent. The '195 and '253 patents are scheduled to expire on the same day as the expiration of the '622 patent (April 12, 2032; absent possible patent term extensions).

The '253 patent includes claims directed to a method of treating moderate to severe acute pain in a human patient by a dose of about 50 mg of IV Tramadol over a time period from 10 minutes to 20 minutes, and administering further doses of tramadol at two to six hour time intervals (each dose being administered intravenously over the same time period).

The ‘195 patent includes claims directed to a method of treating moderate to severe acute pain by administering to a human patient a dose of about 50 mg of IV Tramadol over 10 to 20 minutes, and administering further doses of IV Tramadol at two to six hour time intervals to treat pain in said patient, (each dose administered over 10 to 20 minutes), such that the Cmax does not exceed the Cmax of 100 mg oral tramadol. The term Cmax refers to the maximum plasma concentration of tramadol achieved during a dosing interval. The claims of the ‘195 patent therefore further focus on a goal of the technology — that the blood plasma levels of tramadol resulting from our 50 mg intravenous dose to a patient would not be significantly greater than the blood plasma level of the blood plasma levels of tramadol that are already routinely experienced by patients in the United States who are administered an oral dose of 100 mg tramadol. Tramadol hydrochloride is approved in the United States for oral administration in an amount from 50 to 100 mg administered every four to six hours, not to exceed 400 mg/day.

The ‘253 and ‘195 patents include further claims to the treatment method, including also administering one or more doses of an IV opioid analgesic that is not tramadol as rescue medicine to the patient to treat breakthrough pain. The claims are further directed to the use of the treatment method for postoperative pain, and claims are also directed to the treatment method resulting in a reduction in a side-effect associated with tramadol therapy selected from nausea, vomiting, or both.

We believe that the administration of a 50 mg IV Tramadol dose over the prolonged time interval is efficacious and also may advantageously lead to a lower incidence of side effects and increased drug tolerability. Additionally, we believe that the claims of both the ‘253 and ‘195 patents’ patentably differentiate over all prior art that we are aware of and which was made of record with the USPTO.

Additionally, the License Agreement grants us the rights to a further patent filing to an IV Tramadol dosing regimen which was recently filed with the USPTO and granted prioritized examination. This new patent application (accorded U.S. Application Serial No. 15/163,111; hereinafter referred to as “the ‘111 application”) describes and claims a dosing regimen in which our IV Tramadol product is dosed to a human patient(s) in a manner such that the plasma levels obtained (including but not limited to Cmax and AUC) are very similar to treatment with a 100 mg oral dose of tramadol hydrochloride to a human patient(s) every six hours at steady state. It is believed that this dosing regimen may provide advantages over the commercially available oral doing regimen, and further allows the patient to be stepped down from the IV Tramadol dosing regimen to an oral dosing regimen with less concern about deleterious effects which might occur from a switch from IV to oral analgesic medicine (e.g., as would be the case where the switch to an oral version of the drug provides a much different Cmax and AUC than the IV dose provides at steady state). This new dosing regimen is the result of considerable experimentation by us, and a prior art search has not revealed any similar dosing regimen being used or published with respect to IV Tramadol infusions.

The ‘111 application is now under active review by the USPTO. We believe that the subject matter of this new patent application is new and unobvious and are hopeful of obtaining a new U.S. patent based on this invention sometime in 2017. If granted, we believe that the patent term of a patent granted from this application may extend to at least May 24, 2036 (absent possible patent term extensions).

In sum, we believe that our patent filings will prevent third parties from marketing a generic version of our product without infringing claims of the patent(s) we are seeking. Further, we have conducted clearance searches of U.S. issued and foreign patents, and have not identified any bars to the commercialization of our tramadol technology.

Other Intellectual Property Rights

We depend upon trademarks, trade secrets, and continuing technological advances to develop and maintain our competitive position. We also depend upon the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other

contractors. This knowledge and experience we call "know-how." To help protect our proprietary know-how which is not patentable, and for inventions for which patents may be difficult to enforce, we rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all employees, scientific advisors, consultants, collaborators and other contractors, upon commencement of a relationship with us, to enter into confidentiality agreements, which prohibit the disclosure of confidential information and, in the case of parties other than our research and development collaborators, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business. These agreements are designed to protect our proprietary information and to grant us ownership of technologies that are developed in connection with their relationship with us. These agreements may not, however, provide protection for our trade secrets in the event of unauthorized disclosure of such information.

Supply and Manufacturing

The chemical name for tramadol hydrochloride is cis-2-[(dimethyl amino) methyl]-1-(3-methyoxyphenyl) cyclohexanol hydrochloride. Unless otherwise specified, the term tramadol refers to the racemic mixture of the (±) cis isomers. IV Tramadol (Tramadol Hydrochloride Injection) is a sterile solution formulation of tramadol HCl 50 mg/1 mL, for IV administration. Each unit of IV Tramadol consists of glass ampoules of 50 mg of tramadol HCl and sodium acetate as buffering agent in 1 mL of water for injection or 100 mg of tramadol HCl and sodium acetate as buffering agent in 2 mL of water for injection. The final drug product is stable at room temperature.

We do not own or operate manufacturing facilities for the production of IV Tramadol, nor do we have plans to develop or own manufacturing operations in the foreseeable future. Currently, we have one manufacturer to provide us clinical and commercial supply of IV Tramadol in accordance with cGMP. We also plan to qualify a backup manufacturer. We will be obligated to purchase a minimum amount of final packaged drug product from our current manufacturer over the course of five years commencing upon the approval of our NDA for IV Tramadol. We will pay a fixed per dose unit fee to our current manufacturer in addition to a low single digit royalty on net sales revenue.

We and our manufacturer are and will be subject to extensive government regulation in connection with the manufacture of any pharmaceutical product, including ongoing periodic and unannounced inspections by the FDA, the DEA and corresponding state, European and other foreign agencies to ensure strict compliance with cGMPs and other applicable state, federal and foreign regulations. We do not have control over third party manufacturers' compliance with these regulations and standards, other than through contractual obligations and audit oversight. If they are deemed out of compliance with cGMPs, product recalls could result, inventory could be destroyed, production could be stopped and supplies could be delayed or otherwise disrupted.

If we need to change manufacturers after commercialization, the FDA and some corresponding foreign regulatory agencies must approve these new manufacturers in advance, which will involve testing and additional inspections to ensure compliance with cGMPs and other FDA regulations and standards and may require significant lead times and delay. Furthermore, switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly or on terms acceptable to us, or at all.

Government and Industry Regulations

General

U.S. Drug Development

In the United States, the FDA regulates drugs under the FDCA, and its implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approval and maintaining subsequent compliance with applicable

federal, state and local statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during product development, the approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, voluntary product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution injunctions, fines, consent decrees, refusals of government contracts, restitution, disgorgement or civil and criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us If we fail to manufacture any of our product candidates in sufficient quantities and at acceptable quality and pricing levels, or fail to obtain adequate DEA quotas for controlled substances, or to fully comply with cGMP regulations, we may face delays in the commercialization of this product candidate or be unable to meet market demand, and may be unable to generate potential revenues.

Our product candidates must be approved by the FDA through the NDA process before they may be legally marketed in the United States. We intend to submit our NDAs under the 505(b)(2) regulatory approval pathway. Development and approval of drugs generally involves the following:

- Submission to the FDA of an IND, which must become effective before clinical trials involving humans may begin;
- Approval by an independent institutional review board, or IRB, or ethics committee at each clinical trial site before a trial may be initiated at that site;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations and other good clinical practices, or GCPs;
- Submission of an NDA to the FDA;
- The FDA's decision within 60 days of its receipt of an NDA to accept it for filing and review;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with cGMPs and assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Possible FDA audit of the clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

The nonclinical testing, clinical trials and review process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. The data required to support an NDA are generated in two distinct developmental stages: nonclinical and clinical. The nonclinical development stage generally involves synthesizing the active component, developing the formulation and control procedures and determining the manufacturing process, as well as carrying out non-human toxicology, pharmacology and drug metabolism studies in the laboratory, which may support subsequent clinical testing in humans. In the case of documentation to support a 505(b)(2) NDA, this nonclinical data may be referenced in literature or the FDA's previous findings of safety and efficacy for a listed drug. The sponsor must submit the results of the nonclinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans, and must become effective before clinical trials may begin. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the IND on clinical hold. In such a case, the IND sponsor and

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

The clinical stage of development involves the administration of the product candidate to healthy volunteers and patients under the supervision of qualified investigators, generally physicians not employed by or under the sponsor's control, in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent IRB for each institution where the trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each subject or his or her legal representative and must monitor the clinical trial until completed.

Clinical Trials

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3, and may overlap.

- Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacology, side effect tolerability and safety of the drug.
- Phase 2 clinical trials typically involve studies in disease-affected patients to determine the dose required to produce the desired benefits. At the same time, safety and further pharmacokinetic and pharmacodynamics information is collected, possible adverse effects and safety risks are identified and a preliminary evaluation of efficacy is conducted.
- Phase 3 clinical trials generally involve large numbers of patients at multiple sites and are designed to provide the data necessary to demonstrate the product candidate's safety and effectiveness for its intended use, establish its overall benefit/risk relationship, and provide an adequate basis for approval.

By following the 505(b)(2) regulatory approval pathway, the applicant may reduce some of the burdens of developing a full clinical program by relying on investigations not conducted by the applicant and for which the applicant has not obtained a right of reference, such as prior investigations involving the listed drug. In such cases, some clinical trials may not be required or may be otherwise limited.

Post-approval trials, sometimes referred to as Phase 4, may be conducted after initial marketing approval. These trials are used to gain additional experience from the management of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

Before approval, progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important rate increase of a serious suspected adverse reaction compared to that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the trial is not being conducted in

accordance with the IRB's requirements or the use of the drug raises any safety concerns. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this group may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

There are also requirements governing the reporting of ongoing clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial information, which is publicly available at *www.clinicaltrials.gov*. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. However, there are evolving rules and increasing requirements for publication of all trial-related information, and it is possible that data and other information from trials involving drugs that never garner approval could require disclosure in the future.

Concurrent with clinical trials, companies usually develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing it in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate, and, among other things, a drug manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

NDA and FDA Review Process

The results of nonclinical studies and clinical trials, together with other detailed information, including extensive information on manufacturing and drug composition and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug for one or more specified indications. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMPs to assure and preserve the product's identity, strength, quality and purity. FDA approval of an NDA must be obtained before a drug may be legally marketed in the United States.

Under the PDUFA as amended, each NDA must be accompanied by a user fee. The FDA adjusts the PDUFA user fees on an annual basis. According to the FDA's fee schedule, effective through September 30, 2016, the user fee for an application requiring clinical data, such as an NDA, is $2,374,200. Clinical data, as interpreted by the FDA to assess fees under PDUFA, include (1) study reports or literature reports of what are explicitly or implicitly represented by the applicant to be adequate and well-controlled trials for safety or effectiveness or (2) reports of comparative activity (other than bioequivalence and bioavailability studies), immunogenicity, or efficacy, where those reports are necessary to support a claim of comparable clinical effect. The term does not include bioequivalence and bioavailability studies submitted in support of an NDA. NDAs for which clinical data are not required to demonstrate safety and effectiveness are reduced to half of the amount of the prescribed user fee, or $1,187,100 for 2016. PDUFA also imposes an annual product fee for human drugs ($114,450 per product) and an annual establishment fee ($585,200 per establishment) on facilities used to manufacture prescription drugs. Fee waivers or reductions are available in certain circumstances, including waiver of the application fee for the first application filed by a small business.

The FDA reviews submitted NDAs before it accepts them for filing, and may request additional information rather than accepting the applications. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt. Once the submission is accepted for filing,

the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has ten months from the filing date in which to complete its initial review of a standard NDA and respond to the applicant, and six months from the filing date for an NDA designated for priority review. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs, and the review process is often significantly extended by FDA requests for additional information or clarification.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product to specifications. The FDA may also audit data from clinical trials to ensure compliance with GCP requirements. Additionally, the FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation regarding whether the application should be approved and, if so, under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers them carefully when making decisions. NDAs submitted under Section 505(b)(2) are typically not referred to an Advisory Panel for consideration unless new safety information is revealed in the review cycle. The FDA likely will re-analyze the clinical trial data, which could result in extensive discussions between the FDA and the applicant during the review process. The review and evaluation of an NDA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

After the FDA evaluates an NDA, it will issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes the specific deficiencies in the NDA identified by the FDA, and may require additional clinical data, such as an additional pivotal Phase 3 clinical trial, and other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a Complete Response Letter is issued, the applicant may resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive, and the FDA may interpret data differently than the sponsor interprets the same data.

There is no assurance that the FDA will approve a product candidate for marketing, and the sponsor may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling, or it may condition approval on changes to the proposed labeling. The FDA also may condition approval on the development of adequate controls and specifications for manufacturing and a commitment to conduct post-marketing testing and surveillance to monitor the potential effects of approved products. For example, the FDA may require Phase 4 trials designed to further assess a drug's safety and efficacy.

The FDA may also place other conditions on approval including the requirement for a risk evaluation and mitigation strategy, or REMS, to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution,

prescription or dispensing of products. Marketing approval may be withdrawn for non-compliance with regulatory requirements or if problems occur following initial marketing.

Section 505(b)(2) Regulatory Approval Pathway

Section 505(b)(2) of the FDCA provides an alternate regulatory pathway for approval of a new drug by allowing the FDA to rely on data not developed by the applicant. Specifically, Section 505(b)(2) permits the submission of an NDA where one or more of the investigations relied upon by the applicant for approval was not conducted by or for the applicant and for which the applicant has not obtained a right of reference. The applicant may rely upon published literature and/or the FDA's findings of safety and effectiveness for an approved drug already on the market. Approval or submission of a 505(b)(2) application, like those for abbreviated new drugs, or ANDAs, may be delayed because of patent and/or exclusivity rights that apply to the previously approved drug.

A 505(b)(2) application may be submitted for a new chemical entity, or NCE, when some part of the data necessary for approval is derived from studies not conducted by or for the applicant and when the applicant has not obtained a right of reference. Such data are typically derived from published studies, rather than FDA's previous findings of safety and effectiveness of a previously approved drug. For changes to a previously approved drug however, an applicant may rely on the FDA's finding of safety and effectiveness of the approved drug, coupled with information needed to support the change from the approved drug, such as new studies conducted by the applicant or published data. When based on an approved drug, the 505(b)(2) drug may be approved for all of the indications permitted for the approved drug, as well as any other indication supported by additional data.

Section 505(b)(2) applications also may be entitled to marketing exclusivity if supported by appropriate data and information. As discussed in more detail below, three-year new data exclusivity may be granted to the 505(b)(2) application if one or more clinical investigations conducted in support of the application, other than bioavailability/bioequivalence studies, were essential to the approval and conducted or sponsored by the applicant. Five years of marketing exclusivity may be granted if the application is for an NCE, and pediatric exclusivity is likewise available.

Orange Book Listing and Paragraph IV Certification

For NDA submissions, including those under Section 505(b)(2), applicants are required to list with the FDA certain patents with claims that cover the applicant's product. Upon approval, each of the patents listed in the application is published in *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly referred to as the Orange Book. Any applicant who subsequently files an ANDA or 505(b)(2) NDA that references a drug listed in the Orange Book must certify to the FDA that (1) no patent information on the drug product that is the subject of the application has been submitted to the FDA; (2) such patent has expired; (3) the date on which such patent expires; or (4) such patent is invalid or will not be infringed upon by the manufacture, use or sale of the drug product for which the application is submitted. This last certification is known as a Paragraph IV certification.

If an applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the holder of the NDA for the approved drug and the patent owner once the application has been accepted for filing by the FDA. The NDA holder or patent owner may then initiate a patent infringement lawsuit in response to notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months from the date of the lawsuit, the applicant's successful defense of the suit, or expiration of the patent.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation in which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers.

The Food and Drug Administration Safety and Innovation Act, or FDASIA, which was signed into law on July 9, 2012, amended the FDCA to require that a sponsor who is planning to submit an NDA for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 trial. The initial PSP must include an outline of the pediatric trial(s) that the sponsor plans to conduct, including objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such information and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric trials. The FDA and the sponsor must reach an agreement on the PSP, but the sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials and other clinical development programs.

Post-Marketing Requirements

Following approval, the company and the new product are subject to continuing regulation by the FDA, which include monitoring and recordkeeping activities, reporting of adverse experiences and complying with promotion and advertising requirements, which include prohibitions on the promotion of the drugs for unapproved, or “off-label” uses. Although physicians may prescribe legally available drugs for off-label treatments, manufacturers may not promote such non-FDA approved uses. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use on an on-going basis. Further, if there are any modifications to the drug, including changes to indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a supplemental NDA or new NDA, which may require the applicant to develop additional data or conduct additional nonclinical studies or clinical trials.

The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. These regulations require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMPs. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic, unannounced inspections by the FDA and certain state agencies for compliance with cGMPs and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMPs. The discovery of violative conditions, including failure to conform to cGMPs, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA, including voluntary recalls and product seizures.

Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, untitled or warning letters from the FDA, mandated corrections to advertising or communications to doctors and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product’s approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. New government

requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

U.S. Marketing Exclusivity

The FDCA provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, for a drug product that contains a previously approved NCE if new clinical investigations, other than bioavailability/bioequivalence studies, were essential to the application's approval (*e.g.*, for new indications, dosages or strengths of an existing drug). This three-year exclusivity for new data covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the active agent for the original indication. Furthermore, this exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the nonclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States, which, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protections or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request." The FDA issues a written request for pediatric clinical trials before approval of an NDA only where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

DEA Regulation

Because our product candidate is subject to the Controlled Substances Act, or CSA, we must comply with various requirements set forth by that legislation, as amended, its implementing regulations and as enforced by the DEA. The CSA imposes various registration, record-keeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls, prescription and order form requirements and restrictions on prescription refills for certain kinds of pharmaceutical products. A principal factor for determining the particular requirements of the CSA applicable to a product, if any, is its actual or potential abuse profile. A product may be listed as a Schedule I, II, III, IV or V controlled substance, with Schedule I presenting the highest perceived risk of abuse and Schedule V presenting the least. For example, Schedule I controlled substances have no currently accepted medical use in treatment in the United States and a lack of accepted safety for use under medical supervision. The active ingredient in our product candidate is a Schedule IV controlled substance.

Annual registration is required for any facility that manufactures, distributes, dispenses, imports or exports any controlled substance. The registration is specific to the particular location, activity and controlled substance schedule. For example, separate registrations are needed for import and manufacturing, and each registration will specify which schedules of controlled substances are authorized. Similarly, separate registrations are also required for separate facilities.

The DEA typically inspects a facility to review its security measures prior to issuing a registration and on a periodic basis. Security requirements vary by controlled substance schedule, with the most stringent requirements applying to Schedule I and Schedule II controlled substances. Required security measures include background checks on employees and physical control of inventory through measures such as vaults and inventory reconciliations. Records must be maintained for the handling of all controlled substances, and periodic reports made to the DEA, for example distribution reports for Schedule I and II controlled substances. Reports must also be made for thefts or losses of any controlled substance, and to obtain authorization to destroy any controlled substance.

In addition, a DEA quota system controls and limits the availability and production of controlled substances in Schedule I or II. Distributions of any Schedule I or II controlled substance

must also be accompanied by special order forms, with copies provided to the DEA. Because our products are, and our product candidates are expected to be, regulated as Schedule II controlled substances, they will be subject to the DEA's production and procurement quota scheme. The DEA establishes annually an aggregate quota for how much of a controlled substance may be produced in total in the United States based on the DEA's estimate of the quantity needed to meet legitimate scientific and medicinal needs. The limited aggregate amount that the DEA allows to be produced in the United States each year is allocated among individual companies, which must submit applications annually to the DEA for individual production and procurement quotas. We must receive an annual quota from the DEA in order to produce or procure any Schedule I or Schedule II controlled substance for use in manufacturing of our product and product candidates. The DEA may adjust aggregate production quotas and individual production and procurement quotas from time to time during the year, although the DEA has substantial discretion in whether or not to make such adjustments.

To enforce these requirements, the DEA conducts periodic inspections of registered establishments that handle controlled substances. Failure to maintain compliance with applicable requirements, particularly as manifested in loss or diversion, can result in administrative, civil or criminal enforcement action. The DEA may seek civil penalties, refuse to renew necessary registrations or initiate administrative proceedings to revoke those registrations. In some circumstances, violations could result in criminal proceedings.

In addition to federal scheduling, some drugs may be subject to state-controlled substance regulation and thus more extensive requirements than those determined by the DEA and FDA.

Other Healthcare Laws and Compliance Requirements

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the U.S. Department of Justice, the DEA, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments.

We will also be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and educational programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- The federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either (1) the referral of an individual to a person for furnishing any item or service for which payment is available under a federal health care program, or (2) the purchase, lease, order or recommendation thereof of any good, facility, service or item for which payment is available under a federal health care program;
- The False Claims Act and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, false or fraudulent claims for payment from the federal government or making or using, or causing to be made or used, a false record or statement material to a false or fraudulent claim;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program, obtaining money or property of the health care benefit

program through false representations or knowingly and willingly falsifying, concealing or covering up a material fact, making false statements or using or making any false or fraudulent document in connection with the delivery of, or payment for, health care benefits or services;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- The provision under the ACA commonly referred to as the Sunshine Act, which requires applicable manufacturers of covered drugs, devices, biologics and medical supplies to track and annually report to CMS payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members in applicable manufacturers and group purchasing organizations; and
- State law equivalents of each of the above federal laws, such as the Anti-Kickback Statute and False Claims Act, and state laws concerning security and privacy of health care information, which may differ in substance and application from state-to-state thereby complicating compliance efforts.

The ACA broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. Section 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

As noted above, the federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment from federal programs, including Medicare and Medicaid. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third party reimbursement for our products, and the sale and marketing of our products are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their off-label promotion of drugs. Penalties for such violations could include three times the actual damages sustained by the government, mandatory civil penalties between $10,781 and $21,563 for each separate false claim, exclusion from participation in federal healthcare programs, and the potential implication of various federal criminal statutes. Private individuals also have the ability to bring actions under the federal False Claims Act, or *qui tam* actions, and certain states have enacted laws based on the federal False Claims Act.

Pharmaceutical Coverage, Pricing and Reimbursement

In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of reimbursement from third party payors, including government health administrative authorities, managed care providers, private health insurers and other organizations. Third party payors are increasingly examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy, and, accordingly, significant uncertainty exists as to the

reimbursement status of newly approved therapeutics. Adequate third party reimbursement may not be available for our products to enable us realize an appropriate return on our investment in research and product development. We are unable to predict the future course of federal or state health care legislation and regulations, including regulations that will be issued to implement provisions of the health care reform legislation enacted in 2010, known as the Affordable Care Act. The Affordable Care Act and further changes in the law or regulatory framework could have a material adverse effect on our business.

International Regulation

In addition to regulations in the United States, there are a variety of foreign regulations governing clinical trials and commercial sales and distribution of any product candidates. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval.

Employees

Pursuant to the terms of her Employment Agreement, upon completion of this offering, Lucy Lu will serve as our full-time President and Chief Executive Officer. In addition, David Horin serves in a part-time capacity as our Interim Chief Financial Officer, pursuant to an agreement between us and Chord Advisors, LLC. Dr. Scott A. Reines serves in a part-time capacity as our Interim Chief Medical Officer. None of our employees are represented by labor unions or covered by any collective bargaining agreements. Please see “Executive Compensation” on page 82 for more information on their employment agreements.

Facilities

Our principal facilities consist of leased office space in New York, New York. We believe that this space or replacement office space will be available on commercially reasonable terms.

Legal Proceedings

We are not involved in any litigation that we believe could have a material adverse effect on our financial position or results of operations. There is no action, suit, proceeding, inquiry or investigation before or by any court, public board, government agency, self-regulatory organization or body pending or, to the knowledge of our executive officers, threatened against or affecting our company or our officers or directors in their capacities as such.

MANAGEMENT

Directors and Executive Officers

The following table sets forth certain information about our directors and executive officers.

Name	Age	Position
Lindsay A. Rosenwald, M.D.	61	Executive Chairman of the Board of Directors
Lucy Lu, M.D.	42	Interim President, Chief Executive Officer and Director
Scott A. Reines, M.D., Ph.D.	70	Interim Chief Medical Officer
David Horin, CPA	48	Interim Chief Financial Officer
Michael S. Weiss	51	Director
Neil Herskowitz	60	Director
Jeffrey Paley, MD	49	Director
Akhtar Samad, MD, PhD	57	Director
Jay Kranzler, M.D., PhD	59	Director

Executive Officers

Lindsay A. Rosenwald, M.D. — Executive Chairman of the Board of Directors

Dr. Rosenwald has served as a member of our Board of Directors since inception. Dr. Rosenwald has been a member of the Board of Directors of Fortress since October 2009 and has served as its Chairman, President and Chief Executive Officer since December 2013. He also served as Co-Chairman of the Board of Directors of CB Pharma Acquisition Corp. from their inception in 2014 to June 2016. Dr. Rosenwald also is Co-Portfolio Manager and Partner of Opus Point Partners Management, LLC, an asset management firm in the life sciences industry, which he co-founded in 2009. Prior to that, from 1991 to 2008, he served as the Chairman of Paramount BioCapital, Inc. Over the last 23 years, Dr. Rosenwald has acted as a biotechnology entrepreneur and has been involved in the founding and recapitalization of numerous public and private biotechnology and life sciences companies. Dr. Rosenwald received his B.S. in finance from Pennsylvania State University and his M.D. from Temple University School of Medicine. Based on Dr. Rosenwald's biotechnology and pharmaceutical industry experience and in-depth understanding of our business, the Board of Directors believes that Dr. Rosenwald has the appropriate set of skills to serve as a member of the Board of Directors in light of our business and structure.

Dr. Rosenwald's impressive track record of achievements in leadership positions, including with public companies in the pharmaceutical and medical products industries, led to the conclusion that he should serve as a member of our Board of Directors.

Lucy Lu, M.D. — Interim President and Chief Executive Officer and Director

Dr. Lu has been our Interim President and Chief Executive Officer since inception. Dr. Lu has been the Executive Vice President and Chief Financial Officer of Fortress since February 2012. Prior to working in the biotech industry, Dr. Lu worked for ten years in healthcare-related equity research and investment banking. From February 2007 through January 2012, Dr. Lu was a senior biotechnology equity analyst with Citigroup Investment Research. From 2004 until joining Citigroup, she was with First Albany Capital, serving as Vice President from April 2004 until becoming a Principal of the firm in February 2006. Dr. Lu holds an M.D. degree from the New York University School of Medicine and an M.B.A. from the Leonard N. Stern School of Business at New York University. Dr. Lu obtained a B.A. from the University of Tennessee's College of Arts and Science.

Dr. Lu's extensive leadership and management experience and her experience as the Interim President, Chief Executive Officer of the Company and her deep understanding of the Company's history, business and strategic evolution led to the conclusion that she should serve as a member of our Board of Directors.

Scott A. Reines, M.D., Ph.D. — Interim Chief Medical Officer

Dr. Reines has served as our Interim Chief Medical Officer since January 2016. Dr. Reines been an independent consultant to the pharmaceutical industry since 2008. As Senior Vice President for CNS, Pain, and Translational Medicine at Johnson & Johnson from 2003 to 2008, he oversaw the development and approval of INVEGA and INVEGA SUSTENNA for schizophrenia, NUCYNTA for moderate to severe pain, REMINYL ER for Alzheimer's disease, RISPERDAL CONSTA for schizophrenia and bipolar disorder, RISPERDAL for treatment of the autism, and TOPAMAX for prevention of migraine and seizures. At Johnson & Johnson, he was responsible for all CNS and Pain products, as well as for Clinical Pharmacology and Pharmacogenomics, and was a member of the Johnson & Johnson Pharmaceutical R&D Board of Directors.

Previously, Dr. Reines was Vice President, Clinical Research at Merck from 1988 to 2003, with responsibilities for Psychopharmacology, Neuropharmacology, Gastroenterology, and Ophthalmology. There he led the development of EMEND for prevention of chemotherapy-induced nausea and vomiting, MAXALT for treatment of migraine headache, SINEMET-CR for Parkinson's disease, and TRUSOPT, COSOPT, and TIMOPTIC-XE for prevention of glaucoma. Currently, Dr. Reines consults for biotech, pharmaceutical, and venture firms, is a member of two Scientific Advisory Boards, and Chair of a Data Safety Monitoring Board. He is also a member of two non-profit boards, serving as Vice Chair of the Board of Directors of KidsPeace, a large children's psychiatric healthcare provider, and as a member of the Board of Directors of Heritage Conservancy, which is directed toward land preservation. Dr. Reines also served for two years as co-chair of the Neuroscience Steering Committee, Foundation for NIH Biomarkers Consortium, and spent five years on the National Drug Abuse Advisory Council. He holds a bachelor's degree in chemistry from Cornell University, a PhD in chemistry/molecular biology from Columbia University, and an MD from Albert Einstein College of Medicine. He is Board Certified in Psychiatry and Neurology.

David Horin, CPA — Interim CFO

Mr. Horin has served as our Interim Chief Financial Officer under our agreement with Chord Advisors, LLC since June 2015. Pursuant to such agreement, we pay Chord $7,500 per month for its back office accounting support and accounting policy and financial reporting services that it provides to us, including the services of Mr. Horin. Mr. Horin provides services of approximately 25 hours per month. We do not have information, nor any influence over Mr. Horin's direct compensation from Chord. Mr. Horin has been a Managing Partner of Chord since June 2012. Chord provides accounting advisory services, SEC reporting advisory services, and IPO-readiness services. While at Chord, Mr. Horin has gained extensive experience in financial accounting and SEC reporting for complex business transactions and issues arising from the application of existing or proposed financial accounting guidance. From March 2008 to June 2012, Mr. Horin was the Chief Financial Officer of Rodman & Renshaw Capital Group, Inc., a full-service investment bank dedicated to providing corporate finance, strategic advisory, sales and trading and related services to public and private companies across multiple sectors and regions. From March 2003 through March 2008, Mr. Horin was the Chief Accounting Officer at Jefferies Group, Inc., a full-service global investment bank and institutional securities firm focused on growth and middle-market companies and their investors. Prior to his employment at Jefferies Group, Inc., from 2000 to 2003, Mr. Horin was a Senior Manager in KPMG's Department of Professional Practice in New York, where he advised firm members and clients on technical accounting and risk management matters for a variety of public, international and early growth stage entities. Mr. Horin's education as well as his years of experience as a senior finance executive provide an excellent foundation for his service as our interim Chief Financial Officer. Mr. Horin has a Bachelor of Science degree in Accounting from Baruch College, City University of New York. Mr. Horin is also a Certified Public Accountant.

Non-Executive Directors

Michael S. Weiss

Mr. Weiss has served as a member of our Board of Directors since March 2015 and has served as a director and Executive Vice Chairman of Fortress since February 2014. Mr. Weiss has served as both a director and member of senior management in public and private companies over the past two decades. He also served as Co-Chairman of the Board of Directors of CB Pharma Acquisition Corp. from their inception in 2014 to June 2016. He has also served as Executive Chairman, Interim Chief Executive Officer and President of TG Therapeutics, Inc., a company he founded in 2011. Mr. Weiss is also currently Co-Portfolio Manager and Partner of Opus Point Partners, LLC, which he co-founded in 2009. From 2002 to 2009, Mr. Weiss was the Chairman and Chief Executive Officer of Keryx Biopharmaceuticals, Inc., where he helped the company acquire and develop its lead drug, Auryxia, as well as executed a strategic alliance for Auryxia with Japan Tobacco, Inc. and Torii Pharmaceutical Co., Ltd. worth more than $100 million. Mr. Weiss also served as Chairman of the Board of Directors of National Holdings Corporation from 2011 to 2012. Mr. Weiss' extensive experience founding and managing early stage life science companies makes is the ideal background for a member of our Board of Directors. Mr. Weiss began his professional career as a lawyer with Cravath, Swaine & Moore LLP. He earned his J.D. from Columbia Law School and his B.S. in Finance from The University at Albany.

Mr. Weiss' achievements and wide-ranging experience in the pharmaceutical and medical products sectors led to the conclusion that he should serve as a member of our Board of Directors.

Neil Herskowitz

Mr. Herskowitz joined our Board of Directors in December 2015. Mr. Herskowitz has been a Managing Member of the ReGen Group of Companies since 1998, which include Riverside Contracting LLC, Riverside Claims LLC, ReGen Capital I LLC, ReGen Partners LLC, ReGen Partners I L.P. and, most recently, ReGen Capital Investments LLC and Riverside Claims Investments LLC. He has extensive board membership experience, including as a director of TG Therapeutics, Inc., a public company, from July 2004 to June 2015; Chairman of the Board of Directors of Starting Point Services for Children, a not-for-profit corporation; a Non-Executive Director at Checkpoint Therapeutics, Inc. since August 2015; an Independent Director and Audit Committee Chairman at CB Pharma Acquisition Corporation from November 2014 to May 2016; and previous director positions on the Board of Directors of CytRx Oncology Corporation, Alacrity Biosciences, Inc., Innovive Pharmaceuticals and Chelsea Therapeutics International Ltd. (formerly, Ivory Capital Corp). Mr. Herskowitz earned a B.B.A. in Finance from Bernard M. Baruch College in 1978.

Mr. Herskowitz's background and experience in public accounting and his qualification as an "audit committee financial expert" under SEC rules led to the conclusion that he should serve as a member of our Board of Directors.

Jeffrey Paley, MD.

Dr. Paley joined our Board of Directors in December 2015. Dr. Jeffrey Paley has been an Active Clinician and Consultant in the healthcare industry for the past 18 years, during which time Dr. Paley has consulted for over 30 analysts and portfolio managers in the biotechnology, pharmaceutical, specialty pharmaceutical and medical technology arenas, reviewing the clinical, preclinical and regulatory pedigrees of numerous therapeutics and devices. Prior to his work for the buy-side, Dr. Paley consulted directly for several biotechnology and specialty pharmaceutical companies. Dr. Paley founded Access Medical Associates in 2003, after spending five years on the full-time academic faculty of Weill Cornell Medical College, where he served as a Director of Clinical Research at the Cornell Internal Medicine Associates. At Weill Cornell, Dr. Paley was a Principal or Co-Principal Investigator on several studies of diabetes, hypertension, and cholesterol disorders, including the landmark ACCORD study of intensive hyperglycemia, hypertension and hyperlipidemia management. He has served as a Director of Kellbenx, Retrophin and Remote Radiology Inc. Dr. Paley trained at Harvard Medical School and completed a residency in Internal

Medicine at Massachusetts General Hospital. Dr. Paley has been selected to serve on our Board of Directors based on his experience, including his experience in medicine and clinical trials and in serving as a director of other public companies.

Dr. Paley's medical background and broad business experience in the pharmaceutical industry led to the conclusion that he should serve as a member of our Board of Directors.

Akhtar Samad, MD, PhD

Dr. Samad joined our Board of Directors in December 2015. Akhtar established Symbios Partners in 2008 to address what he perceived as an unmet need in the advisory space — a hybrid strategic advisory and IR consultancy, offering a variety of proprietary services across such areas as clinical and business development, investment thesis and positioning, market intelligence, investor/analyst outreach and financing strategies. He works closely with senior members of client management teams, including CEO, CBO, CMO/CSO, CFO and Director of Communications, to formulate and revise client corporate strategy. Prior to launching Symbios, Akhtar was a Managing Director at Bear Stearns where he directed the small/mid-cap biotechnology equity research team from 2000 – 2008. He is a former academic cancer and genomics researcher, who trained with the co-discoverer of VEGF at Harvard, and completed his medical residency and fellowship at Cornell and the National Cancer Institute. He has been an invited moderator at the Annual Cancer Progress Conferences, and has moderated other oncology and genomics conferences. He received his MD/PhD training at NYU Medical School. Dr. Samad has been selected to serve on our Board of Directors based on his experience, including his experience in biopharmaceutical equity research, strategy and finance.

Dr. Samad's extensive leadership and management experience, including strategic planning, business development, market research, and financing strategies in the biopharmaceutical industry led to the conclusion that he should serve as a member of our Board of Directors.

Jay Kranzler, M.D., PhD

Dr. Kranzler joined our Board of Directors in February 2017. Dr. Kranzler has been a Founder, CEO, Board Member, and Advisor to leading life science companies for over 30 years. He is currently acting as Chief Executive Officer of Regenovation, a regenerative medicine company, and is a Board Member of Methylation Sciences, Pastorus, and ImmunoBrain Checkpoint, all companies focused on developing therapeutics for psychiatric or neurological disorders. Dr. Kranzler started his career at McKinsey & Company in 1985 where he was involved in establishing the Firm's pharmaceutical practice. He served as Chief Executive Officer of Cytel Corporation from 1989 – 1995, a company focused on the development of immunomodulatory drugs. Following Cytel, in 1996, Dr. Kranzler became the Chief Executive Officer of Cypress Bioscience, where he served through 2011. At Cypress, Dr. Kranzler was credited for the development of Savella™ (milnacipran) for the treatment of fibromyalgia. Dr. Kranzler was also Vice President, Head of External R&D Innovation and Worldwide R&D Strategic Investments at Pfizer from 2013 – 2016. During his career, Dr. Kranzler has developed drugs, medical devices, as well as diagnostics, and is the inventor on over 30 patents. Dr. Kranzler graduated from Yale University School of Medicine with MD and PhD degrees in 1985 with a focus in psychopharmacology.

Dr. Kranzler's extensive experience in leadership positions in the pharmaceutical and medical products industries led to the conclusion that he should serve as a member of our Board of Directors.

Family Relationships

There are no family relationship between any director, executive officer or person nominated to become a director or executive officer.

Status as a Controlled Company

Fortress controls a majority of the voting power of our outstanding common stock. As a result, we are a "controlled company" under NASDAQ corporate governance standards. As a controlled company, exemptions under NASDAQ standards will exempt us from certain NASDAQ corporate governance requirements, including the requirements:

- that a majority of our Board of Directors consists of "independent directors," as defined under NASDAQ rules;
- that the compensation of our executive officers be determined, or recommended to the Board of Directors for determination, by majority vote of the independent directors or by a compensation committee comprised solely of independent directors; and
- that director nominees be selected, or recommended to the Board of Directors for selection, by majority vote of the independent directors or by a nomination committee comprised solely of independent directors.

Accordingly, you may not have the same protections afforded to stockholders of companies that are subject to all of NASDAQ's corporate governance requirements. In the event that we cease to be a controlled company, we will be required to comply with these provisions within the transition periods specified in NASDAQ rules.

These exemptions do not modify the independence requirements for our audit committee, and we expect to satisfy the member independence requirement for the audit committee prior to the end of the transition period provided under NASDAQ rules and SEC rules.

Board Committees

Our Board of Directors has established an audit committee and a compensation committee, each of which operates under a charter that has been approved by our Board of Directors.

Our Board of Directors has determined that, upon completion of this offering, all of the members of the audit committee and the compensation committee will be independent as defined under the applicable rules of The NASDAQ Capital Market, including, in the case of all of the members of our audit committee, the independence requirements contemplated by Rule 10A-3 under the Exchange Act. In making such determination, the Board of Directors considered the relationships that each director has with our company and all other facts and circumstances that the Board of Directors deemed relevant in determining director independence, including the beneficial ownership of our capital stock by each director.

Composition of our Board of Directors and Committees

Our Bylaws provide that our Board of Directors must consist of between one and nine directors, and such number of directors within this range may be determined from time to time by resolution of our Board of Directors or our stockholders. Currently, we have seven directors.

Our Bylaws also provide that our directors may be removed with or without cause by the affirmative vote of the holders of at least a majority of the shares then entitled to vote at an election of directors. An election of our directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

Our current and future executive officers and significant employees serve at the discretion of our Board of Directors. Our Board of Directors has decided to form a compensation and an audit committee.

Audit Committee

The members of our audit committee are Neil Herskowitz, Jeffrey Paley, M.D. and Akhtar Samad, M.D., PhD. Neil Herskowitz chairs the audit committee. Upon the closing of this offering, our audit committee's responsibilities will include:

- appointing, approving the compensation of and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- overseeing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our Board of Directors has determined that Mr. Herskowitz is an "audit committee financial expert" as defined by applicable SEC rules.

Compensation Committee

The members of our compensation committee are Jay Kranzler, M.D., PhD, Jeffrey Paley, M.D. and Akhtar Samad, M.D., PhD. Dr. Kranzler chairs the compensation committee. Upon the closing of this offering, our compensation committee's responsibilities will include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our chief executive officer;
- reviewing and approving, or making recommendations to our Board of Directors with respect to, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our Board of Directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" disclosure required by SEC rules; and
- preparing the compensation committee report required by SEC rules.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serves as a member of the Board of Directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our Board of Directors or our compensation committee.

Director Compensation

None of our directors received any compensation for their service as a director since our inception February 9, 2015 through December 31, 2016. Our Compensation Committee will evaluate director compensation following the completion of this offering.

Communicating with the Board of Directors

Our Board of Directors has established a process by which stockholders can send communications to the Board of Directors. You may communicate with the Board of Directors as a group, or to specific directors, by writing to our Corporate Secretary, at our offices located at 2 Gansevoort Street, 9th Floor, New York, NY 10014. The Corporate Secretary will review all such correspondence and regularly forward to our Board of Directors a summary of all correspondence and copies of all correspondence that, in the opinion of the Corporate Secretary, deals with the functions of the Board of Directors or committees thereof or that he otherwise determines requires their attention. Directors may at any time review a log of all correspondence we receive that is addressed to members of our Board of Directors and request copies of any such correspondence. Concerns relating to accounting, internal controls, or auditing matters may be communicated in this manner. These concerns will be immediately brought to the attention of our Board of Directors and handled in accordance with procedures established by our Board of Directors.

Code of Ethics

We adopted a Code of Ethics that applies to all directors, officers and employees. Our Code of Ethics is available on our website at *www.avenuetx.com.* A copy of our code of ethics will also be provided to any person without charge, upon written request sent to us at our offices located at 2 Gansevoort Street, 9th Floor, New York, NY 10014.

EXECUTIVE COMPENSATION

The Summary Compensation Table below sets forth information regarding the compensation awarded to or earned by our named executive officers during the years ended December 31, 2015 and 2016.

Summary Compensation Table for 2016

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards ($) (1)	Total ($)
Lucy Lu (2)	2016	181,132 (2)	$ 135,800 (5)	27,875	344,805
Chief Executive Officer	2015	40,155 (2)		20,047	60,202
Scott A. Reines	2016	43,175 (3)		—	43,175
Interim Chief Medical Officer	2015	16,040 (3)		—	16,040
David J. Horin	2016	50,000 (4)		—	50,000
Interim Chief Financial Officer	2015	13,500 (4)		—	13,500

(1) Reflects the aggregate grant date fair value of restricted stock granted during the fiscal year calculated in accordance with FASB ASC Topic 718. See Note 8 to our audited financial statements for the year ended December 31, 2016, included elsewhere in this prospectus, for a discussion of the assumptions made by us in determining the grant date fair value of our equity awards.

(2) Dr. Lu's employment will commence upon the completion of this offering. The amount reported represents the pro rata portion of Dr. Lu's annual salary at Fortress based the percentage of her time devoted to us. From February 2015 through December 31, 2015, Dr. Lu spent approximately 27% of her time devoted to us and from January 1, 2016 through December 31, 2016, Dr. Lu spent approximately 53% of her time devoted to us.

(3) The amount reported represents the amount paid to Dr. Reines during 2015 and 2016 pursuant to our Consulting Agreement with him, at an hourly rate of $400 per hour. He provided us with approximately 40 hours of work in 2015 and approximately 106 hours of work in 2016.

(4) Mr. Horin spends approximately 10% of his time on matters related to us. The amount reported represents 10% of the amount paid to Chord during 2015 and 2016, for services rendered. We do not have information or any influence over Mr. Horin's direct compensation from Chord.

(5) The amount reported represents the bonus amount to be paid to Dr. Lu during 2017, earned in 2016 pursuant to her Employment Agreement with Fortress. Her 2016 bonus goals were all in connection with the development of IV Tramadol. As such, 100% of her bonus was charged to us.

Compensation Arrangements for Executive Officers

On June 10, 2015, we entered into an Employment Agreement with Lucy Lu, M.D., or the Employment Agreement, to serve as our Interim President and Chief Executive Officer upon the completion of this offering. Under the terms of Dr. Lu's Employment Agreement, upon the completion of this offering, Dr. Lu's base salary will be equal to $395,000 per year. Dr. Lu's base salary may be reduced only in connection with a company-wide decrease in executive compensation. Dr. Lu is also eligible to receive an annual discretionary bonus, not to exceed 50% of her base salary, if certain financial, clinical development, and/or business milestones are met in the discretion of Board of Directors. Such milestones will be established annually by mutual agreement between Dr. Lu and the Board of Directors. Prior to her execution of the Employment Agreement, Ms. Lu was awarded 1,000,000 shares of our common stock pursuant to a Restricted Stock Issuance Agreement between us and Ms. Lu, dated May 28, 2015. Dr. Lu's employment with us is at will and may be terminated by us at any time and for any reason. However, under the terms of the Employment Agreement, if we terminate Dr. Lu's employment without cause (as defined in the Employment Agreement) or if Dr. Lu resigns her employment for good reason (as defined in the Employment Agreement), Dr. Lu will be entitled to receive the following:

- cash severance equal to her annual salary, paid over a period of twelve months;
- payment of the premiums to continue health care coverage for Dr. Lu and her eligible dependents under COBRA for up to twelve months;

- a pro rata share of her annual bonus, to be paid when and if such bonus would have been paid under the Employment Agreement; and
- immediate vesting of the portion of her unvested equity awards with respect to the number of shares that would have vested if Dr. Lu had remained employed for one year after the termination date, or full vesting of all unvested equity awards if such termination occurs on or within six months following a Change of Control (as defined in the Employment Agreement).

If Dr. Lu's employment is terminated due to her Death or Complete Disability (as defined in the Employment Agreement), she shall be entitled to receive the following:

- cash severance equal to her annual salary, paid over a period of ninety days;
- a pro rata share of her annual bonus, to be paid when and if such bonus would have been paid under the Employment Agreement; and
- immediate vesting of the portion of her unvested equity awards with respect to the number of shares that would have vested if Dr. Lu had remained employed for one year after the termination date.

The term of the Employment Agreement begins when this registration statement is declared effective. Dr. Lu is also the Chief Financial Officer of Fortress.

Although no formal written agreement has been entered into with Dr. Rosenwald, our Executive Chairman, we have orally agreed to pay Dr. Rosenwald a cash salary equal to $50,000 per year for services as our executive chairman, provided that no payments will be made to Dr. Rosenwald until we complete a third party financing, which includes this offering.

On January 25, 2016, we entered into a First Amendment to our Consulting Agreement with Dr. Reines, which we originally entered into on July 22, 2015. The original agreement provided that Dr. Reines would provide general consulting services relating to statistical, clinical and other strategic issues. Under the agreement, as amended, Dr. Reines will serve as our Interim Chief Medical Officer and will remain an independent contractor. Pursuant to the agreement, we pay Dr. Reines $400.00 per hour for all services provided to us. We entered into a Second Amendment with Dr. Reines in August 2016 that extends the agreement for a period of two years, followed by automatic renewal for successive one-year periods, unless earlier terminated.

On June 12, 2015, we entered into an agreement with Chord, under which Mr. Horin will serve as our Interim Chief Financial Officer and Chord will provide back office accounting support as well as accounting policy and financial reporting for us. We paid Chord an advisory fee of $5,000 per month prior to the public filing of this registration statement and have agreed to pay $7,500 per month thereafter. The arrangement can be terminated by either party upon 30 days written notice. Chord also provides advisory services to Fortress. We do not have information or any influence over Mr. Horin's direct compensation from Chord.

Outstanding Equity Awards at December 31, 2016

The following table provides information regarding outstanding stock awards held by our named executive officers as of December 31, 2016. We have not granted any stock options to our named executive officers.

		Stock Awards			
Name	Grant Date	Number of Shares or Units of Stock That Have Not Vested (#) (1)	Market Value of Shares or Units of Stock That Have Not Vested ($) (1)	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#) (2)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units of Other Rights That Have Not Vested ($) (2)
Lucy Lu	6/10/2015	375,000	$ 72,750	500,000	$ 97,000

(1) Represents restricted stock awards vesting annually on June 10, 2016, 2017 and 2018, contingent on Dr. Lu's continuing service, based upon a valuation conducted by us.

(2) Represents restricted stock awards vesting based upon achievement of goals and objectives relating to the development of IV Tramadol. This amount is based upon a valuation conducted by us.

Employee Benefit and Incentive Plans

We do not maintain any deferred compensation, retirement, pension or profit sharing plans. Our Board of Directors has adopted an incentive plan, the material terms of which are described below, allowing for the grant of equity and cash-based awards to our employees and directors.

Director Compensation

None of our directors received any compensation for their service as a director since our inception February 9, 2015 through December 31, 2016. Following the completion of this offering, our Compensation Committee will determine the compensation of our independent directors, if any.

Equity Incentive Plan

2015 Incentive Plan

On December 10, 2015, our Board of Directors adopted the Avenue Therapeutics, Inc. 2015 Incentive Plan, or the 2015 Plan. The material terms of the 2015 Plan are described below. As set forth below, the 2015 Plan will be administered by the Compensation Committee. The Compensation Committee has not yet been formed, but it will be formed before any necessary actions to be taken by the Compensation Committee with respect to the 2015 Plan are taken.

Purpose. The purpose of the 2015 Plan is to promote our success by linking the personal interests of our employees, officers, directors and consultants to those of our stockholders, and by providing participants with an incentive for outstanding performance.

Permissible Awards. The 2015 Plan authorizes the Compensation Committee to grant awards in any of the following forms:

- options to purchase shares of our common stock, which may be nonstatutory stock options or incentive stock options under the Internal Revenue Code. The exercise price of an option granted under the 2015 Plan may not be less than the fair market value of our common stock on the date of grant. Stock options granted under the 2015 Plan may not have a term longer than ten years;

- stock appreciation rights, or SARs, which give the holder the right to receive the excess, if any, of the fair market value of one share of our common stock on the date of exercise, over the base price of the stock appreciation right. The base price of a SAR may not be less than the fair market value of our common stock on the date of grant. SARs granted under the 2015 Plan may not have a term longer than ten years;
- restricted stock, which is subject to restrictions on transferability and subject to forfeiture on terms set by the Compensation Committee;
- restricted stock units, which represent the right to receive shares of our common stock (or an equivalent value in cash or other property) in the future, based upon the attainment of stated vesting or performance goals set by the Compensation Committee;
- deferred stock units, which represent the right to receive shares of our common stock (or an equivalent value in cash or other property) in the future, generally without any vesting or performance restrictions;
- other stock-based awards in the discretion of the Compensation Committee, including unrestricted stock grants; and
- cash-based awards in the discretion of the Compensation Committee, including cash-based performance awards.

All awards will be evidenced by a written award certificate between us and the participant, which will include such provisions as may be specified by the Compensation Committee. Dividend equivalent rights, which entitle the participant to payments in cash or property calculated by reference to the amount of dividends paid on the shares of stock underlying an award, may be granted with respect to awards other than options or SARs.

Awards to Non-Employee Directors. Awards granted under the 2015 Plan to our non-employee directors will be made only in accordance with the terms, conditions and parameters of a plan, program or policy for the compensation of non-employee directors as in effect from time to time. The Compensation Committee may not make discretionary grants under the 2015 Plan to non-employee directors. The maximum aggregate number of shares associated with any award granted under the 2015 Plan in any calendar year to any one non-employee director is 100,000.

Shares Available for Awards; Adjustments. Subject to adjustment as provided in the 2015 Plan, the aggregate number of shares of our common stock reserved and available for issuance pursuant to awards granted under the 2015 Plan is 2,000,000. Shares subject to awards that are canceled, terminated, forfeited, settled in cash, withheld to satisfy exercise prices or tax withholding obligations or otherwise not issued for any reason, including by reason of failure to achieve maximum performance goals, will again be available for awards under the 2015 Plan. In the event of a nonreciprocal transaction between us and our stockholders that causes the per share value of our common stock to change (including, without limitation, any stock dividend, stock split, spin-off, rights offering, or large nonrecurring cash dividend), the share authorization limits under the 2015 Plan will be adjusted proportionately, and the Compensation Committee must make such adjustments to the 2015 Plan and awards as it deems necessary, in its sole discretion, to prevent dilution or enlargement of rights immediately resulting from such transaction.

Administration. The 2015 Plan will be administered by the Compensation Committee. The Compensation Committee will have the authority to grant awards; designate participants; determine the type or types of awards to be granted to each participant and the number of awards to be granted and the number of shares or dollar amount to which an award will relate and the terms and conditions thereof; prescribe the form of award; establish, adopt or revise any rules and regulations as it may deem advisable to administer the 2015 Plan; make all other decisions and determinations that may be required under the 2015 Plan and amend the 2015 Plan. Our Board of Directors may at any time administer the 2015 Plan. If it does so, it will have all the powers of the

Compensation Committee under the 2015 Plan. In addition, our Board of Directors or Compensation Committee may expressly delegate to a special committee some or all of the Compensation Committee's authority, within specified parameters, to grant awards to eligible participants who, at the time of grant, are not executive officers or directors.

Limitations on Transfer; Beneficiaries. No award will be assignable or transferable by a participant other than by will or the laws of descent and distribution; provided, however, that nonstatutory stock options may be transferred without consideration to members of a participant's immediate family, to trusts in which such immediate family members have more than 50% of the beneficial interest, to foundations in which such immediate family members (or the participant) control the management of assets, and to any other entity (including limited partnerships and limited liability companies) in which the immediate family members (or the participant) own more than 50% of the voting interest; and provided, further, that the Compensation Committee may permit other transfers (other than transfers for value) where the Compensation Committee concludes that such transferability does not result in accelerated taxation, does not cause any option intended to be an incentive stock option to fail to qualify as such, and is otherwise appropriate and desirable, taking into account any factors deemed relevant, including without limitation, any state or federal tax or securities laws or regulations applicable to transferable awards. A participant may, in the manner determined by the Compensation Committee, designate a beneficiary to exercise the rights of the participant and to receive any distribution with respect to any award upon the participant's death.

Treatment of Awards upon a Change in Control. Unless otherwise provided in an award certificate or any special plan document governing an award, upon the occurrence of a change in control of our company, (i) all outstanding options, SARs and other awards in the nature of rights that may be exercised will become fully exercisable, (ii) all time-based vesting restrictions on outstanding awards will lapse; and (iii) the payout opportunities attainable under all outstanding performance-based awards will vest based on target performance and the awards will pay out on a pro rata basis, based on the time elapsed prior to the change in control.

Discretionary Acceleration. The Compensation Committee may, in its discretion, accelerate the vesting and/or payment of any awards for any reason, subject to certain limitations under Section 409A of the Internal Revenue Code. The Compensation Committee may discriminate among participants or among awards in exercising such discretion.

Certain Transactions. Upon the occurrence or in anticipation of certain corporate events or extraordinary transactions, the Compensation Committee may also make discretionary adjustments to awards, including settling awards for cash, providing that awards will become fully vested and exercisable, providing for awards to be assumed or substituted, or modifying performance targets or periods for awards.

Termination and Amendment. The 2015 Plan will terminate on the tenth anniversary of its adoption, or, if the stockholders approve an amendment to the 2015 Plan that increases the number of shares subject to the 2015 Plan, the tenth anniversary of the date of such approval, unless earlier terminated by our Board of Directors or Compensation Committee. Our Board of Directors, Audit Committee or Compensation Committee may, at any time and from time to time, terminate or amend the 2015 Plan, but if an amendment to the 2015 Plan would constitute a material amendment requiring stockholder approval under applicable listing requirements, laws, policies or regulations, then such amendment will be subject to stockholder approval. No termination or amendment of the 2015 Plan may adversely affect any award previously granted under the 2015 Plan without the written consent of the participant. Without the prior approval of our stockholders, and except as otherwise permitted by the anti-dilution provisions of the 2015 Plan, the 2015 Plan may not be amended to permit us to directly or indirectly reprice, replace or repurchase "underwater" options or SARs.

The Compensation Committee may amend or terminate outstanding awards. However, such amendments may require the consent of the participant and, unless approved by the stockholders or otherwise permitted by the anti-dilution provisions of the 2015 Plan, (i) the exercise price or base price of an option or SAR may not be reduced, directly or indirectly, (ii) an option or SAR may not be cancelled in exchange for cash, other awards, or options or SARS with an exercise price or base price that is less than the exercise price or base price of the original option or SAR, or otherwise, (iii) we may not repurchase an option or SAR for value (in cash or otherwise) from a participant if the current fair market value of the shares of our common stock underlying the option or SAR is lower than the exercise price or base price per share of the option or SAR, and (iv) the original term of an option or SAR may not be extended.

Prohibition on Repricing. As indicated above under "Termination and Amendment," outstanding stock options and SARs cannot be repriced, directly or indirectly, without the prior consent of our stockholders. The exchange of an "underwater" option or stock appreciation right (i.e., an option or stock appreciation right having an exercise price or base price in excess of the current market value of the underlying stock) for cash or for another award would be considered an indirect repricing and would, therefore, require the prior consent of our stockholders.

Certain Federal Tax Effects

The following discussion is limited to a summary of the U.S. federal income tax provisions relating to the grant, exercise and vesting of awards under the 2015 Plan and the subsequent sale of common stock acquired under the 2015 Plan. The tax consequences of awards may vary depending upon the particular circumstances, and it should be noted that the income tax laws, regulations and interpretations thereof change frequently. Additional taxes, including state, local, and foreign tax laws, may apply.

Nonstatutory Stock Options. There typically will be no federal income tax consequences to the optionee or to us upon the grant of a nonstatutory stock option under the 2015 Plan. When the optionee exercises a nonstatutory option, however, he or she will recognize ordinary income in an amount equal to the excess of the fair market value of our common stock received upon exercise of the option at the time of exercise over the exercise price, and we will typically be allowed a corresponding deduction. Any gain that the optionee realizes when he or she later sells or disposes of the option shares will be short-term or long-term capital gain, depending on how long the shares were held.

Incentive Stock Options. There typically will be no federal income tax consequences to the optionee or to us upon the grant or exercise of an incentive stock option. If the optionee holds the option shares for the required holding period of at least two years after the date the option was granted or one year after exercise, the difference between the exercise price and the amount realized upon sale or disposition of the option shares will be long-term capital gain or loss, and we will not be entitled to a federal income tax deduction on such amount. If the optionee disposes of the option shares in a sale, exchange, or other disqualifying disposition before the required holding period ends, he or she will recognize taxable ordinary income in an amount equal to the excess of the fair market value of the option shares at the time of exercise (or, if less, the amount realized on the disposition of the shares) over the exercise price, and we would typically be allowed a federal income tax deduction equal to such amount. While the exercise of an incentive stock option does not result in current taxable income, the excess of the fair market value of the option shares at the time of exercise over the exercise price will be an item of adjustment for purposes of determining the optionee's alternative minimum taxable income.

Stock Appreciation Rights. A participant receiving a stock appreciation right typically will not recognize income, and we will not be allowed a tax deduction, at the time the award is granted. When the participant exercises the stock appreciation right, the amount of cash and the fair market value of any shares of our common stock received will be ordinary income to the participant and we will typically be allowed as a corresponding federal income tax deduction at that time.

Restricted Stock. Unless a participant makes an election to accelerate recognition of income to the date of grant as described below, the participant will not recognize income, and we will not be allowed a tax deduction, at the time a restricted stock award is granted, provided that the award is subject to restrictions on transfer and is subject to a substantial risk of forfeiture. When the restrictions lapse, the participant will recognize ordinary income equal to the fair market value of our common stock as of that date (less any amount he or she paid for the stock), and we will typically be allowed a corresponding federal income tax deduction at that time, subject to limitations in certain circumstances. If the participant files an election under Code Section 83(b) within 30 days after the date of grant of the restricted stock, he or she will recognize ordinary income as of the date of grant equal to the fair market value of the stock as of that date (less any amount paid for the stock), and we will typically be allowed a corresponding federal income tax deduction, subject to limitations in certain circumstances at that time. Any future appreciation in the stock will be taxable to the participant at capital gains rates. However, if the stock is later forfeited, the participant will not be able to recover the tax previously paid pursuant to the Section 83(b) election. To the extent unrestricted dividends are paid during the restricted period under the applicable award agreement, any such dividends will be taxable to the participant at ordinary income tax rates and will be deductible by us unless the participant has made a Section 83(b) election, in which case the dividends will thereafter be taxable to the participant as dividends and will not be deductible by us.

Stock Units. A participant typically will not recognize income, and we will not be allowed a tax deduction, at the time a stock unit award is granted. Upon receipt of shares of our common stock (or the equivalent value in cash) in settlement of a stock unit award, a participant will recognize ordinary income equal to the fair market value of our common stock or other property as of that date, and we will typically be allowed a corresponding federal income tax deduction at that time, subject to limitations in certain circumstances.

Cash-Based Performance Awards. A participant will not recognize income, and we will not be allowed a tax deduction, at the time a cash-based performance award is granted (for example, when the performance goals are established). Upon receipt of cash in settlement of the award, the participant will recognize ordinary income equal to the cash received, and we will typically be allowed a corresponding federal income tax deduction at that time, subject to limitations in certain circumstances.

RELATIONSHIPS AND RELATED TRANSACTIONS

The following is a summary of each transaction or series of similar transactions since our inception to which we were or are a party and that:

- the amount involved exceeded or exceeds $120,000 or is greater than 1% of our total assets; and
- any of our directors or executive officers, any holder of 5% of our capital stock or any member of their immediate family had or will have a direct or indirect material interest.

Founders Agreement and Management Services Agreement with Fortress

Effective as of February 17, 2015, we entered into a Founders Agreement with Fortress, pursuant to which Fortress assigned to us all of its right and interest under Fortress' license agreement with Revogenex for IV Tramadol. As consideration for the Founders Agreement, we assumed $3.0 million in debt that Fortress accumulated under the NSC Note for the IV Tramadol license, of which $2.0 million represents the initial payment in February 2015 and $1.0 million the payment made in June 2015. As additional consideration for the transfer of rights under the Founders Agreement, we will also: (i) issue annually to Fortress, on the anniversary date of the Founders Agreement, shares of common stock equal to 2.50% of our fully-diluted outstanding equity at the time of issuance; (ii) pay an equity fee in shares of common stock, payable within five business days of the closing of any equity or debt financing that occurs after the effective date of the Founders Agreement and ending on the date when Fortress no longer has majority voting control of our voting equity, equal to 2.50% of the gross amount of any such equity or debt financing; and (iii) pay a cash fee equal to 4.5% of our annual net sales, payable on an annual basis, within 90 days of the end of each calendar year. In the event of a change in control (as it is defined in the Founders Agreement), we will pay a one-time change in control fee equal to five times the product of (i) monthly net sales for the 12 months immediately preceding the change in control and (ii) 4.5%.

On September 13, 2016, we entered into an Amended and Restated the Founders Agreement, or the A&R Founders Agreement, with Fortress. The A&R Founders Agreement eliminated the annual equity fee in connection with the original agreement and added a term of 15 years, which upon expiration automatically renews for successive one-year periods unless terminated by Fortress or a change in control occurs. Concurrently with the A&R Founders Agreement, we entered into an Exchange Agreement whereby we exchanged Fortress's 7.0 million Class A common shares for approximately 7.5 million common shares and 250,000 Class A Preferred shares. In connection with the issuance of Class A Preferred shares, Fortress will receive an annual stock dividend.

Effective as of February 17, 2015, we entered into a Management Services Agreement, or the MSA, with Fortress and each of our then current directors and officers who are directors or officers of Fortress to provide services to us pursuant to the terms of the MSA. Pursuant to the terms of the MSA, for a period of five years, Fortress will render advisory and consulting services to us. Services provided under the MSA may include, without limitation, (i) advice and assistance concerning any and all aspects of our operations, clinical trials, financial planning and strategic transactions and financings and (ii) conducting relations on behalf of us with accountants, attorneys, financial advisors and other professionals. We are obligated to utilize clinical research services, medical education, communication and marketing services and investor relations/public relation services of companies or individuals designated by Fortress, provided those services are offered at market prices. However, we are not obligated to take or act upon any advice rendered from Fortress and Fortress will not be liable for any of our actions or inactions based upon their advice. Fortress and its affiliates, including all members of our Board of Directors, have been contractually exempt from fiduciary duties to us relating to corporate opportunities. In consideration for the services rendered pursuant to the MSA, we will pay Fortress an annual consulting fee of $0.5 million, or the Annual Consulting Fee, payable in advance in equal quarterly installments on the first business day of each calendar quarter in each year, provided, however,

that such Annual Consulting Fee shall be increased to $1.0 million for each calendar year in which we have net assets in excess of $100 million at the beginning of the calendar year. For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) to December 31, 2015, we recognized approximately $500,000 and $417,000, respectively, in expense on the Statement of Operations related to the MSA. Effective March 16, 2017, we have the option to pay the Annual Consulting Fee in cash or to issue shares of our common stock.

Issuance of Common Shares to Fortress

In connection with the Founders Agreement, for the period ended December 31, 2015, we recorded an annual equity fee of $40,000 representing the 228,750 shares of our common stock at $0.176 per share. The annual equity fee represents 2.5% of our outstanding shares, issuable on the anniversary date of the Founders Agreement. As such, on February 17, 2016, the shares were issued. On September 13, 2016, in connection with the A&R Founders Agreement, this annual equity fee was eliminated.

For the period ended December 31, 2016, in connection with the 250,000 Class A Preferred shares, we recorded an expense of $49,000, representing the expense related to the Preferred A stock dividend. The expense is related to the 250,595 common shares issuable to Fortress on the anniversary date of the A&R Founders Agreement, representing 2.5% of our outstanding shares at December 31, 2016, at $0.194 per share or $49,000.

Fortress Note

Effective March 15, 2015, we entered into a future advance promissory note with Fortress, or the Fortress Note, in which Fortress agreed to provide a working capital line of credit until we have a third party financing. Interest on the Fortress Note is being accrued at 8% per annum and will be payable to Fortress on the day after the end of each calendar quarter following the first third party financing. All principal and accrued interest under the Fortress Note is payable on demand following the first third party financing. This Fortress Note can be pre-paid at any time in cash or through the assumption of Fortress' indebtedness NSC or other similar indebtedness. Effective March 17, 2017, the interest rate was reduced to 2.0%. As of December 31, 2016, the Fortress Note totaled approximately $2.8 million.

Consulting Agreement with Chord Advisors, LLC

On June 12, 2015, we entered into a full-service consulting agreement with Chord Advisors, LLC, or Chord, to provide advisory accounting services to us. Under the terms of the agreement, we will pay Chord $5,000 per month prior to becoming a public company and $7,500 per month thereafter to perform back office accounting functions, accounting analysis and financial reporting. Either party upon 30-days written notice can terminate the agreement. In addition to these services, Mr. Horin, a Managing Partner of Chord, will serve as our Interim Chief Financial Officer. Chord also provides advisory accounting services to Fortress under a separate agreement.

NSC Note and Financings

In September 2016, Fortress acquired through a tender offer 56.6% of National Holdings, Inc., or National. We hold a $3.0 million note in favor of NSC Biotech Venture Fund I, LLC for which National Securities, Inc., or NSC, a subsidiary of National, received a 10% placement fee upon issuance of the Note to Fortress. In addition, upon the completion of a third party raise of five times the NSC Note, we will issue a warrant to NSC as the placement agent equal to 25% of the outstanding debt.

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of our common stock as of March 21, 2017 by the following:

- each of our directors and named executive officers;
- all of our directors and named executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power of that security, including options and warrants that are currently exercisable or exercisable within 60 days of March 21, 2017. Shares of our common stock issuable pursuant to stock options are deemed outstanding for computing the percentage of the person holding such options and the percentage of any group of which the person is a member but are not deemed outstanding for computing the percentage of any other person. Except as indicated by the footnotes below, we believe, based on the information furnished to us, that the persons named in the table below have sole voting and investment power with respect to all shares of common stock shown that they beneficially own, subject to community property laws where applicable. The information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Section 13(d) and 13(g) of the Securities Act.

Our calculation of the percentage of beneficial ownership prior to this offering is based on 9,974,405 shares of common stock outstanding as of March 21, 2017. Our calculation of the percentage of beneficial ownership after this offering is based on shares of common stock outstanding immediately after the closing of this offering, assuming no exercise of outstanding options and no exercise of the underwriters' options to purchase additional shares of our common stock.

Unless otherwise indicated, the address for each director and executive officer listed is: c/o Avenue Therapeutics, Inc., 2 Gansevoort Street, 9th Floor, New York, NY 10014.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned	
		Before Offering	After Offering
Lucy Lu, M.D.	1,000,000	10.0%	
Michael S. Weiss	500,000 (1)	5.0% (1)	
Lindsay A. Rosenwald, M.D.	500,000 (1)	5.0% (1)	
David J. Horin	0	0.0%	
Scott A. Reines, M.D., Ph.D.	0	0.0%	
Neil Herskowitz	0	0.0%	
Jeffrey Paley	0	0.0%	
Akhtar Samad, M.D., PhD	0	0.0%	
Jay Kranzler, M.D., PhD	0	0.0%	
All executive officers and directors as a group (9 persons)	1,000,000 (2)	10.0% (2)	
5% or Greater Stockholders:			
Fortress Biotech, Inc. (3)	8,974,405	89.5%	

(1) Mr. Weiss and Dr. Rosenwald each have warrants convertible into 500,000 shares of our common stock. These warrants were issued by Fortress and are convertible into shares of our common stock that are owned by Fortress. These do not represent equity compensation by us to either Mr. Weiss or Dr. Rosenwald.

(2) The total calculation for all executive officers and directors as a group does not include Mr. Weiss' and Dr. Rosenwald's warrants, which have not yet been exercised.

(3) Excludes 250,000 Class A Preferred shares owned by Fortress. See "Relationships and Related Transactions" for a description of Fortress' ownership.

DESCRIPTION OF CAPITAL STOCK

The following description summarizes the material terms of our capital stock as of the date of this registration statement. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description of our capital stock, you should refer to our Second Amended and Restated Certificate of Incorporation and our Bylaws, and to the provisions of applicable Delaware law.

Upon the closing of this initial offering, our authorized capital stock will consist of 50,000,000 shares of common stock, with $0.0001 par value, and 2,000,000 shares of Preferred Stock, with $0.0001 par value, of which 250,000 have been designated as Class A Preferred Stock and the remainder are undesignated Preferred Stock. Only our common stock is being registered hereby.

As of December 31, 2016, we had issued and outstanding 10,023,810 shares of our common stock held by three stockholders of record. We have not issued any options or other securities under our 2015 Incentive Plan.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our Board of Directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Class A Preferred Stock

Class A Preferred Stock is identical to our common stock other than as to voting rights, the election of directors for a definite period, conversion rights and the PIK Dividend right (as described below). On any matter presented to our stockholders for their action or consideration at any meeting of our stockholders (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Class A Preferred Stock will be entitled to cast for each share of Class A Preferred Stock held by such holder as of the record date for determining stockholders entitled to vote on such matter, the number of votes that is equal to one and one-tenth (1.1) times a fraction, the numerator of which is the sum of (A) the shares of outstanding common stock and (B) the whole shares of common stock in to which the shares of outstanding Class A Preferred Stock are convertible and the denominator of which is the number of shares of outstanding Class A Preferred Stock, or the Class A Preferred Stock Ratio. Thus, the Class A Preferred Stock will at all times constitute a voting majority.

For a period of ten years from the date of the first issuance of shares of Class A Preferred Stock, or the Class A Director Period, the holders of record of the shares of Class A Preferred Stock (or other capital stock or securities issued upon conversion of or in exchange for the Class A Preferred Stock), exclusively and as a separate class, shall be entitled to appoint or elect the majority of our directors, or the Class A Directors. Thus, the Class A Preferred Stock will be entitled to elect the majority of the Board of Directors during the Class A Director Period.

The holders of the outstanding shares of Class A Preferred Stock shall receive on each February 17, each a PIK Dividend Payment Date, after the original issuance date of the Class A

Preferred Stock until the date all outstanding Class A Preferred Stock is converted into common stock or redeemed (and the purchase price is paid in full), pro rata per share dividends paid in additional fully paid and nonassessable shares of common stock, such dividend being herein called PIK Dividends, such that the aggregate number of shares of common stock issued pursuant to such PIK Dividend is equal to 2.5% of our fully-diluted outstanding capitalization on the date that is one business day prior to any PIK Dividend Payment Date, or PIK Record Date. In the event the Class A Preferred Stock converts into common stock, the holders shall receive all PIK Dividends accrued through the date of such conversion.

Finally, each share of Class A Preferred Stock is convertible, at the option of the holder, into one fully paid and nonassessable share of common stock, or the Conversion Ratio, subject to certain adjustments.

Undesignated Preferred Stock

The undesignated Preferred Stock may be issued from time to time in one or more series. Our Board of Directors is authorized to determine or alter the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions, if any), the redemption price or prices, the liquidation preferences and other designations, powers, preferences and relative, participating, optional or other special rights, if any, and the qualifications, limitations and restrictions granted to or imposed upon any wholly unissued series of Preferred Stock, and to fix the number of shares of any series of Preferred Stock (but not below the number of shares of any such series then outstanding).

Anti-Takeover Provisions

We are subject to Section 203 of the Delaware General Corporation Law, or the DGCL. Subject to certain exemptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our Board of Directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Listing

We have applied for listing on the NASDAQ Capital Market under the trading symbol "ATXI." No assurance can be given that our application will be approved.

Transfer Agent and Registrar

Upon the closing of this offering, the transfer agent and registrar for our common stock will be VStock Transfer, LLC.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a summary of the material United States federal income tax consequences relating to the acquisition, ownership and disposition of our common stock as of the date hereof. Except where noted, this summary deals only with our common stock that is held as a capital asset (within the meaning of Section 1221 of the Internal Revenue Code of 1986, as amended, or the Code, by a "non-U.S. holder" (as defined below).

For purposes of this summary, a "non-U.S. holder" means a beneficial owner of our common stock (other than a partnership or any other entity treated as a partnership for United States federal income tax purposes) that is not for United States federal income tax purposes any of the following:

- an individual citizen or resident of the United States;
- a corporation (or any other entity treated as a corporation for United States federal income tax purposes) created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- an estate the income of which is subject to United States federal income taxation regardless of its source; or
- a trust if it (1) is subject to the primary supervision of a court within the United States and one or more United States persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable United States Treasury regulations ("Treasury Regulations") to be treated as a United States person.

This summary is based upon provisions of the Code and Treasury Regulations, administrative rulings and judicial decisions currently in effect, all as of the date hereof and all subject to change at any time, possibly with retroactive effect, or to different interpretation by the Internal Revenue Service ("IRS"). This summary does not address all aspects of United States federal taxes and does not address any foreign, state, local or other tax considerations that may be relevant to non-U.S. holders in light of their personal circumstances. In addition, this summary does not represent a detailed description of the United States federal income tax consequences applicable to holders that are subject to special treatment under the United States federal income tax laws (including a holder that is a United States expatriate, "controlled foreign corporation," "passive foreign investment company," "real estate investment trust," "regulated investment company," dealer in securities or currencies, financial institution, tax-exempt entity, insurance company, person holding our common stock as part of a hedging, integrated, conversion or constructive sale transaction or a straddle, trader in securities that elects to use a mark-to-market method of accounting, person liable for the alternative minimum tax, person who acquired our common stock as compensation for services, or a partnership or other pass-through entity, or partner in a partnership or beneficial owner of a pass-through entity that holds our common stock for United States federal income tax purposes). We cannot provide assurance that a change in law will not alter significantly the tax considerations that we describe in this summary.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds our common stock, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. Non-U.S. holders that are partners of a partnership holding our common stock should consult their tax advisors.

Non-U.S. holders considering the purchase of our common stock should consult their own tax advisors concerning the particular United States federal income and estate tax consequences of the ownership of our common stock, as well as the consequences arising under the laws of any other taxing jurisdiction.

Distribution on our common stock

As indicated in the "Dividend Policy" section of this prospectus, we have never paid cash dividends on any of our capital stock and currently intend to retain our future earnings, if any, to fund the development and growth of our business.

In the event that we do make a distribution, distributions paid on our common stock will be treated as dividends to the extent paid out of current or accumulated earnings and profits, as determined under United States federal income tax principles. Dividends paid to a non-U.S. holder of our common stock generally will be subject to United States federal withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. However, dividends that are effectively connected with the conduct of a trade or business by the non-U.S. holder within the United States (and, if required by an applicable income tax treaty, are attributable to a United States permanent establishment) are not subject to United States federal withholding tax, provided certain certification and disclosure requirements are satisfied. Instead, such dividends are subject to United States federal income tax on a net income basis in the same manner as if the non-U.S. holder were a United States person as defined under the Code. Any such effectively connected dividends received by a foreign corporation may, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

A non-U.S. holder of our common stock who wishes to claim the benefit of an applicable treaty rate and avoid backup withholding, as discussed below, for dividends will be required (a) to complete IRS Form W-8BEN or W-8BEN-E (or other applicable form) and certify under penalty of perjury that such holder is not a "United States person" as defined under the Code and is eligible for treaty benefits or (b) if the common stock is held through certain foreign intermediaries, to satisfy the relevant certification requirements of applicable Treasury Regulations. Special certification and other requirements apply to certain non-U.S. holders that are pass-through entities rather than corporations or individuals.

A non-U.S. holder of our common stock eligible for a reduced rate of United States withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by filing an appropriate claim for refund with the IRS. Dividend distributions to non-U.S. holders would also be subject to the rules concerning FATCA, as further discussed below.

Gain on disposition of our common stock

Subject to the discussion below under the heading "FACTA withholding requirements," any gain realized on the disposition of our common stock by a non-U.S. holder generally will not be subject to United States federal income tax unless:

- the gain is effectively connected with a trade or business of the non-U.S. holder in the United States (and, if required by an applicable income tax treaty, is attributable to a United States permanent establishment of the non-U.S. holder);
- the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of that disposition, and certain other conditions are met; or
- we are or have been a "United States real property holding corporation" for United States federal income tax purposes at any time during the shorter of the five-year period ending on the date of the disposition or such non-U.S. holder's holding period for our common stock and such non-U.S. holder held (at any time during the shorter of the five-year period ending on the date of the disposition or such non-U.S. holder's holding period) more than 5% of our common stock.

An individual non-U.S. holder described in the first bullet point immediately above will be subject to tax on the net gain derived from the sale under regular graduated United States federal income tax rates. If a non-U.S. holder that is a foreign corporation falls under the first bullet point immediately above, it will be subject to tax on its net gain in the same manner as if it were a

"United States person" as defined under the Code and, in addition, may, under certain circumstances, be subject to a branch profits tax equal to 30% of its effectively connected earnings and profits or at such lower rate as may be specified by an applicable income tax treaty.

We believe we have not been and are not currently a "United States real property holding corporation" for United States federal income tax purposes; however, no assurance can be given that we are not or will not become one in the future. If, however, we are or become a "United States real property holding corporation," so long as our common stock continues to be regularly traded on an established securities market, only a non-U.S. holder who holds, or held (at any time during the shorter of the five-year period ending on the date of disposition or the non-U.S. holder's holding period) more than 5% of our common stock will be subject to United States federal income tax on the disposition of the common stock. No assurance can be given, however, that our common stock continues to be treated as regularly traded on an established securities market for applicable federal income tax purposes. Non-U.S. holders should consult their own tax advisors about the consequences that could result if we are, or become, a "United States real property holding corporation."

Information reporting and backup withholding

We must report annually to the IRS and to each non-U.S. holder the amount of dividends paid to such holder and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available to the tax authorities in the country in which the non-U.S. holder resides under the provisions of an applicable income tax treaty.

A non-U.S. holder will be subject to backup withholding for dividends paid to such holder unless such holder certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that such holder is a "United States person" as defined under the Code), or such holder otherwise establishes an exemption.

Information reporting and, depending on the circumstances, backup withholding will apply to the proceeds of a sale of our common stock within the United States or conducted through certain United States-related financial intermediaries, unless the beneficial owner certifies under penalty of perjury that it is a non-U.S. holder (and the payor does not have actual knowledge or reason to know that the beneficial owner is a "United States person" as defined under the Code), or such owner otherwise establishes an exemption.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a non-U.S. holder's United States federal income tax liability provided the required information is furnished to the IRS.

FATCA withholding requirements

Under Section 1471 through Section 1474 of the Code and the Treasury Regulations promulgated and official guidance issued thereunder, collectively, FATCA, the relevant withholding agent may be required to withhold 30% of any dividends on our common stock, and on the gross proceeds from the sales of our common stock on or after January 1, 2019, in each case, to (i) a foreign financial institution unless such foreign financial institution agrees to verify, report and disclose its U.S. accountholders and meets certain other specified requirements or (ii) a non-financial foreign entity that is the beneficial owner of the payment unless such entity certifies that it does not have any substantial United States owners or provides the name, address and taxpayer identification number of each substantial United States owner and such entity meets certain other specified requirements. In certain cases, the relevant foreign financial institution or non-financial foreign entity may qualify for an exemption from, or be deemed to be in compliance with, these rules. Certain countries have entered into intergovernmental agreements with the United States that supplement and modify these rules. Non-U.S. holders should consult their own tax advisors regarding the impact of FATCA on their ownership and disposition of our common stock.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options, or the anticipation of these sales, could materially and adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of equity or equity-related securities.

As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below. Nevertheless, sales of a substantial number of shares of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could materially and adversely affect the prevailing market price of our common stock. Although we have applied to list our common stock on the NASDAQ Capital Market, we cannot assure you that there will be an active market for our common stock.

Upon the closing of this offering, we will have outstanding an aggregate of shares of our common stock, assuming (i) the underwriters do not exercise their over-allotment option, and (ii) no options outstanding as of , 2017 are exercised.

Of the shares to be outstanding immediately after the closing of this offering, we expect that the shares to be sold in this offering will be freely tradable without restriction under the Securities Act unless purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining shares of our common stock outstanding after this offering will be "restricted securities" under Rule 144, and we expect that substantially all of these restricted securities will be subject to the 180-day lock-up period under the lock-up agreements as described below. These restricted securities may be sold in the public market only if registered or pursuant to an exemption from registration, such as Rule 144 or Rule 701 under the Securities Act.

Rule 144

Affiliate Resales of Restricted Securities

In general, subject to the lock-up restrictions described below, beginning 90 days after the effective date of the registration statement, of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering; or
- the average weekly trading volume in our common stock on the NASDAQ Capital Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the SEC and the NASDAQ Capital Market concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

Non-Affiliate Resales of Restricted Securities

In general, subject to the lock-up restrictions described above, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the

three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us.

If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Upon expiration of the 180-day lock-up period described below, approximately shares of our common stock will be eligible for sale under Rule 144, including shares eligible for resale immediately upon the closing of this offering as described above. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

Rule 701

Rule 701 under the Securities Act generally allows a stockholder who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been an affiliate of ours during the immediately preceding 90 days to sell these shares in reliance upon Rule 144, but without being required to comply with the public information, holding period, volume limitation, or notice provisions of Rule 144. Rule 701 also permits affiliates of ours to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701 and until expiration of the 180-day lock-up period described below.

Subject to the 180-day lock-up period described below, approximately shares of our common stock will be eligible for sale in accordance with Rule 701.

Lock-Up Agreements

We, each of our directors and executive officers and holders of all of our outstanding shares of common stock have agreed that, without the prior written consent of on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 180 days after the date of this prospectus, subject to extension in specified circumstances:

- sell, offer to sell, contract or agree to sell, hypothecate, pledge, grant any option to purchase or otherwise dispose of or agree to dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exchangeable or exercisable for shares of our common stock, or publicly announce an intention to do the same;
- establish or increase a put equivalent position or liquidate or decrease a call equivalent position with respect to any shares of our common stock or any securities convertible into or exchangeable or exercisable for shares of our common stock, or publicly announce an intention to do the same;
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock or any securities convertible into or exchangeable or exercisable for shares of our common stock, whether such transaction is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise, or publicly announce an intention to do the same; or
- make any demand for or exercise any right with respect to the registration of any shares of our common stock or any securities convertible into or exchangeable or exercisable for shares of our common stock.

The lock-up restrictions, specified exceptions and the circumstances under which the 180-day lock-up period may be extended are described in more detail under “Underwriting.”

UNDERWRITING

Raymond James & Associates, Inc. is acting as representative of each of the underwriters named below, with Raymond James & Associates, Inc. serving as sole book-runner and National Securities Corp. serving as manager in this offering. Subject to the conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us the number of shares of our common stock set forth opposite its name below:

Name	Number of Shares
Raymond James & Associates, Inc.	
National Securities Corp.	
Total:	

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' option described below. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may be increased or the offering may be terminated.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers at that price less a concession not in excess of $ per share. After the initial offering of the shares of common stock, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

Option to Purchase Additional Shares of Common Stock

We have granted the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

Discounts and Expenses

The following table shows per share and total public offering prices, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional shares of common stock.

	Per Share	Total No Exercise	Total Full Exercise
Initial public offering price			
Underwriting discounts and commissions			
Proceeds, before expenses			

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $.

We have agreed to reimburse Raymond James & Associates, Inc. for out-of-pocket accountable expenses up to a maximum of $150,000 upon completion of this offering.

Indemnification

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

Lock-Up Agreements

In connection with this offering, subject to specified exceptions, we and each of our directors and officers, and all of our stockholders have agreed that, subject to certain exceptions, without the prior written consent of Raymond James & Associates, Inc. as representative on behalf of the underwriters, we and they will not, subject to customary exceptions, during the period ending six months after the date of the final prospectus relating to this offering:

- offer, sell, agree to offer or sell, solicit offers to purchase, grant any call option or purchase any put option with respect to, pledge, encumber, assign, borrow or otherwise dispose of or transfer, any shares of our stock or options, warrants or other securities with respect to our stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our common stock.

The preceding restrictions apply without regard to whether any such transaction described above is to be settled by delivery of common stock or other securities, in cash or otherwise. In addition, we and each such person agree that, without the prior written consent of the representative, we and each such person will not, during the period ending six months after the date of the final prospectus relating to this offering, make any demand for, or exercise any right with respect to, the registration of any shares of common stock or any security convertible into or exercisable or exchangeable for common stock.

The six month restricted period described in the preceding paragraph will be extended if, during any period that we are not an emerging growth company:

- during the last 17 days of the 90 day restricted period we issue an earnings release or material news event relating to us occurs, or
- prior to the expiration of the 90 day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180 day period, in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the announcement of the material news or material event.

Stabilization

Until this offering is completed, rules of the SEC may limit the ability of the underwriters and various selling group members to bid for and purchase the shares of our common stock. As an exception to these rules and in accordance with Regulation M under the Exchange Act, the underwriters may engage in activities that stabilize, maintain or otherwise affect the price of our common stock in order to facilitate the offering of the common stock, including: short sales; syndicate covering transactions; imposition of penalty bids; and purchases to cover positions created by short sales.

Stabilizing transactions may include making short sales of shares of our common stock, which involve the sale by the underwriters of a greater number of shares than it is required to purchase in this offering and purchasing shares of common stock from us by exercising the option or in the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option referred to above, or may be “naked” shorts, which are short positions in excess of that amount.

Each underwriter may close out any covered short position either by exercising its option, in whole or in part, or by purchasing shares of common stock in the open market after the distribution has been completed. In making this determination, each underwriter will consider,

among other things, the price of shares of our common stock available for purchase in the open market compared to the price at which the underwriter may purchase shares of our common stock pursuant to the underwriters' option.

A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of shares of our common stock in the open market after pricing that could adversely affect investors who purchased in this offering. To the extent that the underwriters create a naked short position, they will purchase shares of our common stock in the open market to cover the position after the pricing of this offering.

The underwriters also may impose a penalty bid on selling group members. This means that if the underwriters purchase shares of our common stock in the open market in stabilizing transactions or to cover short sales, the underwriters can require the selling group members that sold those shares as part of this offering to repay the selling concession received by them.

As a result of these activities, the price of shares of our common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them without notice at any time. The underwriters may carry out these transactions on the NASDAQ Capital Market or otherwise.

The underwriters are not required to engage in these activities and may end any of these activities at any time.

Relationships and Conflict of Interest

Certain of the underwriters and their affiliates may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates, and for the selling stockholders and their affiliates, in the ordinary course of their business, for which they will receive customary fees and commissions, as applicable, and reimbursement for out-of-pocket expenses. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account 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.

In September 2016, our parent company Fortress acquired 56.6% of National Holdings, Inc., which owns National Securities Corp., through a tender offer. National Securities Corp. is a FINRA member and will participate in this offering. Accordingly, the offering is subject to the provisions of FINRA Rule 5121 regarding conflicts of interest and will be conducted in accordance with the requirements of Rule 5121. Raymond James & Associates, Inc. does not have a conflict of interest and will be primarily responsible for managing the offering and performing the usual due diligence.

Listing

We have applied for listing on the NASDAQ Capital Market under the trading symbol "ATXI." No assurance can be given that our application will be approved.

LEGAL MATTERS

Certain legal matters will be passed upon for us by Alston & Bird LLP, New York, New York. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York, is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The financial statements as of December 31, 2016 and 2015 and for the year ended December 31, 2016 and the period from February 9, 2015 (inception) to December 31, 2015 included in this prospectus and elsewhere in this registration statement have been so included in reliance on the report of BDO USA, 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 have filed with the SEC, Washington, D.C. 20549, a registration statement on Form S-1 under the Securities Act with respect to the common stock offered hereby. This prospectus does not contain all of the information set forth in the registration statement and the exhibits and schedules thereto. For further information with respect to us and our common stock, reference is made to the registration statement and the exhibits and any schedules filed therewith. Statements contained in this prospectus as to the contents of any contract or other document referred to are not necessarily complete and in each instance, if such contract or document is filed as an exhibit, reference is made to the copy of such contract or other document filed as an exhibit to the registration statement, each statement being qualified in all respects by such reference. A copy of the registration statement, including the exhibits and schedules thereto, may be read and copied at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains an Internet site at *www.sec.gov*, from which interested persons can electronically access the registration statement, including the exhibits and any schedules thereto.

As a result of the offering, we will become subject to the full informational requirements of the Exchange Act. We will fulfill our obligations with respect to such requirements by filing periodic reports and other information with the SEC. You will be able to inspect and copy these reports and proxy and information statements and other information at the addresses set forth above. We intend to furnish our stockholders with annual reports containing financial statements certified by an independent public accounting firm. We also maintain an Internet site at *www.avenuetx.com.* Our website and the information contained therein or connected thereto shall not be deemed to be incorporated into this prospectus or the registration statement of which it forms a part.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

Board of Directors and Stockholders
Avenue Therapeutics, Inc.
New York, New York

We have audited the accompanying balance sheets of Avenue Therapeutics, Inc. as of December 2016 and 2015 and the related statements of operations, stockholders' deficit, and cash flows for the year ended December 31, 2016 and the period from February 9, 2015 (inception) to December 31, 2015. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States) and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Avenue Therapeutics, Inc. at December 31, 2016 and 2015, and the results of its operations and its cash flows for the year ended December 31, 2016 and the period from February 9, 2015 (inception) to December 31, 2015**,** in conformity with accounting principles generally accepted in the United States of America.

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As described in Note 1 to the financial statements, the Company has suffered recurring losses from operations and has a net capital deficiency that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

/s/ BDO USA, LLP
Boston, Massachusetts
March 6, 2017

AVENUE THERAPEUTICS, INC.

BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2016	December 31, 2015
ASSETS		
Current Assets:		
Cash	$ 197	$ 14
Total Assets	**$ 197**	**$ 14**
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current Liabilities:		
Accounts payable and accrued expenses	$ 506	$ 491
Accrued expenses – related party	1,348	511
Interest payable	57	—
Accrued interest – related party	346	165
Notes payable – related party	2,848	1,165
NSC notes payable, short-term	1,000	—
Derivative warrant liability	314	114
Total current liabilities	6,419	2,446
Convertible notes payable, at fair value	200	—
NSC notes payable, long-term (net of debt discount of $174 and $297, respectively)	1,826	2,703
Total Liabilities	8,445	5,149
Commitments and Contingencies		
Stockholders' Deficit		
Preferred Stock ($0.0001 par value), 2,000,000 shares authorized		
Class A Preferred Stock, 250,000 and 0 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—	—
Common Stock ($0.0001 par value), 50,000,000 shares authorized		
Class A Common Stock, 0 and 7,000,000 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—	1
Common shares; 9,773,810 and 2,150,000 shares issued and outstanding as of December 31, 2016 and 2015, respectively	1	—
Common stock issuable, 250,595 and 228,750 shares as of December 31, 2016 and 2015, respectively	49	40
Additional paid-in capital	105	50
Accumulated deficit	(8,403)	(5,226)
Total Stockholders' Deficit	(8,248)	(5,135)
Total Liabilities and Stockholders' Deficit	**$ 197**	**$ 14**

The accompanying notes are an integral part of these financial statements.

AVENUE THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	For The Year Ended December 31, 2016	For The Period from February 9, 2015 (Inception) through December 31, 2015
Operating expenses:		
Research and development	$ 1,331	$ 961
Research and development – licenses acquired	49	3,040
General and administration	997	842
Loss from operations	(2,377)	(4,843)
Interest expense	420	215
Interest expense – related party	192	168
Change in fair value of warrant liabilities	188	—
Net Loss	**$ (3,177)**	**$ (5,226)**
Net loss per common share outstanding, basic and diluted	$ (0.37)	$ (0.64)
Weighted average number of common shares outstanding, basic and diluted	8,581,578	8,107,209

The accompanying notes are an integral part of these financial statements.

AVENUE THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS' DEFICIT
(In thousands, except share amounts)

	Class A Preferred Shares		Class A Common Shares		Common Shares		Common shares issuable	Additional paid-in capital	Accumulated deficit	Total Stockholders' deficit
	Shares	Amount	Shares	Amount	Shares	Amount				
Issuance of Class A common shares to Fortress on February 9, 2015	—	$ —	7,000,000	$ 1	—	$ —	$ —	$ (1)	$ —	$ —
Issuance of common shares to Fortress on February 9, 2015	—	—	—	—	1,000,000	—	—	—	—	—
Issuance of common shares for services	—	—	—	—	150,000	—	—	22	—	22
Share based compensation	—	—	—	—	1,000,000	—	—	29	—	29
Common shares issuable to Fortress per Founders Agreement	—	—	—	—	—	—	40	—	—	40
Net loss	—	—	—	—	—	—	—	—	(5,226)	(5,226)
Balance at December 31, 2015	**—**	**$ —**	**7,000,000**	**$ 1**	**2,150,000**	**$ —**	**$ 40**	**$ 50**	**$ (5,226)**	**$ (5,135)**
Share based compensation	—	—	—	—	—	—	—	28	—	28
Issuance of common shares – Founders Agreement	—	—	—	—	252,560	—	(40)	45	—	5
Conversion Class A common shares to Class A preferred shares and common shares	250,000	—	(7,000,000)	(1)	7,471,250	1	—	—	—	—
Common shares issuable to Fortress per Founders Agreement	—	—	—	—	—	—	49	—	—	49
Retirement of common shares	—	—	—	—	(100,000)	—	—	(18)		(18)
Net loss	—	—	—	—	—	—	—	—	(3,177)	(3,177)
Balance at December 31, 2016	**250,000**	**$ —**	**—**	**$ —**	**9,773,810**	**$ 1**	**$ 49**	**$ 105**	**$ (8,403)**	**$ (8,248)**

The accompanying notes are an integral part of these financial statements.

AVENUE THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS
(In thousands)

	For The Year Ended December 31, 2016	For The Period from February 9, 2015 (Inception) through December 31, 2015
Cash flows from operating activities:		
Net loss	$ (3,177)	$ (5,226)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share based compensation	28	29
Issuance of common shares for services	—	22
Research and development-licenses acquired, expensed	—	3,000
Common shares issuable – Founders Agreement	49	40
Common shares issued – Founders Agreement	5	—
Change in fair value of warrant liabilities	188	—
Financing fees expensed related to convertible notes, at fair value	58	—
Non-cash financing fees expensed related to convertible notes, at fair value	12	—
Debt discount amortization	123	73
Changes in operating assets and liabilities:		
Accounts payable and accrued expenses	15	491
Accrued expenses – related party	829	511
Interest payable	57	—
Accrued interest – related party	181	165
Net cash used in operating activities	(1,632)	(895)
Cash flows from investing activities:		
Purchase of research and development licenses	—	(3,000)
Net cash used in investing activities	—	(3,000)
Cash flows from financing activities:		
Proceeds from convertible note, at fair value	200	—
Financing fees expensed related to convertible notes, at fair value	(58)	—
Proceeds from NSC notes payable	—	3,000
Payment of debt issue costs associated with NSC Note	—	(256)
Proceeds from notes payable – related party	1,673	1,165
Net cash provided by financing activities	1,815	3,909
Net change in cash	183	14
Cash, beginning of period	14	—
Cash, end of period	**$ 197**	**$ 14**
Non-cash investing and financing activities:		
Issuance of Class A common shares to Fortress on February 9, 2015	$ —	$ 1
Warrant liability associated with NCS debt	$ —	$ 114
Retirement of common shares	$ 18	$ —
Conversion Class A common shares to Class A preferred shares and common shares	$ 1	$ —
Supplemental disclosure of cash flow information:		
Cash paid for interest	$ 183	$ 60

The accompanying notes are an integral part of these financial statements.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 1 — Organization, Plan of Business Operations and Going Concern Consideration

Avenue Therapeutics, Inc. (the "**Company**" or "**Avenue**") was incorporated in Delaware on February 9, 2015, as a wholly owned subsidiary of Fortress Biotech, Inc. ("**Fortress**"), to develop and market pharmaceutical products for the acute care setting in the United States. The company will focus on developing its product candidate, an intravenous ("**IV**") formulation of tramadol HCI ("**IV Tramadol**"), for moderate to moderately severe postoperative pain.

Intravenous formulation of Tramadol HCI ("IV Tramadol")

In February 2015, Fortress purchased an exclusive license to an intravenous ("**IV**") formulation of Tramadol for the U.S. market from Revogenex Ireland Ltd ("**Revogenex**"), a privately held company in Dublin, Ireland. Fortress made an upfront payment of $2.0 million to Revogenex upon execution of the exclusive license, with an additional $1.0 million paid 120 days later, on June 17, 2015. Under the terms of the agreement, Revogenex is eligible to receive additional milestone payments upon the achievement of certain development milestones, in addition to royalty payments for sales of the product. Tramadol is a centrally acting synthetic opioid analgesic for moderate to moderately severe pain and is available as immediate release or extended-release tablets in the United States.

Fortress transferred the Revogenex license and all other rights and obligations of Fortress under the License Agreement to Avenue pursuant to the Assignment and Assumption Agreement effective as of February 17, 2015. Per the terms of the agreement, the Company assumed $3.0 million in debt (see Note 6).

Avenue plans to initiate a Phase 3 development program of IV Tramadol for the management of postoperative pain in 2016 following completion of a pharmacokinetics or PK study.

On February 9, 2015, Lucy Lu, M.D. was appointed to serve as the Company's Interim President and Chief Executive Officer. Under the terms of Dr. Lu's Employment Agreement, dated as of June 10, 2015 (the "**Employment Agreement**"), upon the Company becoming a public company, Dr. Lu will serve as the Company's full-time President and Chief Executive Officer and receive base salary equal to $395,000 per year. Dr. Lu's base salary may be reduced only in connection with a Company-wide decrease in executive compensation. Dr. Lu is also eligible to receive an annual discretionary bonus, not to exceed 50% of her base salary, if certain financial, clinical development, and/or business milestones are met at the discretion of the Board. Prior to her execution of the Employment Agreement, Dr. Lu was granted 1,000,000 shares of the Company's common stock pursuant to a Restricted Stock Issuance Agreement between the Company and Dr. Lu, dated June 10, 2015. Dr. Lu's employment with the Company is at will and may be terminated by the Company at any time and for any reason. However, under the terms of the Employment Agreement, Dr. Lu will be entitled to cash severance payments if the Company terminates her employment without cause (as defined in the Employment Agreement) or if Dr. Lu resigns her employment for good reason (as defined in the Employment Agreement). Dr. Lu also serves as the Chief Financial Officer for Fortress.

The expense allocations to Avenue, which represent Lucy Lu's executive compensation in accordance with the terms of her employment agreement with Fortress, have been paid by Fortress and allocated by the Company between Avenue and Fortress by allocating time spent on Avenue projects versus time spent on Fortress projects. The allocations were based on assumptions that management believes are reasonable; however, these allocations are not necessarily indicative of the costs and expenses that would have resulted if Avenue had been operating as a stand-alone entity. For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) through December 31, 2015, the allocated expenses related to Lucy Lu were approximately $336,800 and $94,500, respectively.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 1 — Organization, Plan of Business Operations and Going Concern Consideration – (continued)

Going Concern Consideration

As of December 31, 2016, the Company's working capital deficit was approximately $6.2 million, and the Company's stockholders' deficit was approximately $8.2 million. Further, the Company expects to continue to incur significant costs in pursuit of its financing plans, developments plans and acquisition plans. The Company will need to raise capital in order to proceed with its plans to conduct a Phase 3 development program. The Company's plan to raise capital may not be successful. These factors, among others, raise substantial doubt about the Company's ability to continue as a going concern. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Note 2 — Significant Accounting Policies

Basis of Presentation

The Company's financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("**GAAP**"). The Company has no subsidiaries.

The financial statements may not be indicative of future performance and may not reflect what their results of operations, financial position, and cash flows would have been had Avenue operated as an independent entity. Certain estimates, including allocations from Fortress, have been made to provide financial statements for stand-alone reporting purposes. All inter-company transactions between Fortress and Avenue are classified as accrued expenses — related party in the financial statements. The Company believes that the assumptions underlying the financial statements are reasonable. The cost allocation methods applied to certain common costs include the following:

- Specific identification. Where the amounts were specifically identified to Avenue, they were classified accordingly.
- Reasonable allocation. Where the amounts were not clearly or specifically identified, management determined if a reasonable allocation method could be applied.

The financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("**U.S. GAAP**") and are stated in U.S. dollars.

The acquisition of the IV Tramadol license and the assumption of liabilities in connection with this license was accounted for as a transaction among businesses under common control. Because the license and assumption of liabilities met the definition of a business (as defined in ASC 805), the transfer of the business represented a transfer among entities under common control which should be accounted for at carrying amount with retrospective adjustment of prior period financial statements similar to the manner in which a pooling-of-interest was accounted for under APB 16*, Business Combinations.* Given this, the acquisition of the license by Fortress (and transferred to Avenue) represented a Research and Development expenditure which should be expensed pursuant to ASC 730 *Research and Development*.

Results of operations for the period in which the acquisition occurred are reported as though the acquisition had occurred at the beginning of the period. Accordingly, results of operations, presented in the financial statements, for period February 9, 2015 (Inception) through December 31, 2015 are comprised of operations of the Company.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

Cash and Cash Equivalents

The Company considers all short-term investments with an original maturity of three months or less when purchased to be cash equivalents. There were no cash equivalents at December 31, 2016 and 2015.

Use of Estimates

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

Research and Development

Research and development costs are expensed as incurred. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made. Upfront and milestone payments due to third parties that perform research and development services on the Company's behalf will be expensed as services are rendered or when the milestone is achieved. Costs incurred in obtaining technology licenses are charged to research and development expense if the technology licensed has not reached technological feasibility and has no alternative future use.

Research and development costs primarily consist of personnel related expenses, including salaries, benefits, travel, and other related expenses, stock-based compensation, payments made to third parties for license and milestone costs related to in-licensed products and technology, payments made to third party contract research organizations for preclinical and clinical studies, investigative sites for clinical trials, consultants, the cost of acquiring and manufacturing clinical trial materials, costs associated with regulatory filings and patents, laboratory costs and other supplies.

Costs incurred in obtaining technology licenses are charged to research and development expense if the technology licensed has not reached commercial feasibility and has no alternative future use. The licenses purchased by the Company require substantial completion of research and development, regulatory and marketing approval efforts in order to reach commercial feasibility and has no alternative future use. Accordingly, the total purchase price for the licenses acquired are reflected as research and development — licenses acquired on the Company's Statement of Operations.

Annual Equity Fee

Prior to the September 2016 amendment to the Founder's Agreement (the "**Amended and Restated Founders Agreement**"), Fortress was entitled to an annual fee on each anniversary date equal to 2.5% of the fully diluted outstanding equity of the Company, payable in Avenue Common Stock ("**Annual Equity Fee**"). The annual equity fee was part of consideration payable for formation of the Company and identification of certain assets.

The Company recorded the Annual Equity Fee in connection with the Founders Agreement with Avenue as contingent consideration. Contingent consideration is recorded when probable and reasonably estimable. The Company's future share prices cannot be estimated due to the nature of its assets and the Company's stage of development. Due to these uncertainties, the Company has concluded that it is unable to reasonably estimate the contingent consideration until shares are

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

actually issued on February 17 of each year. Because the issuance of shares on February 17, 2016 occurred prior to the issuance of the December 31, 2015 financial statements, the Company recorded approximately $40,000 in research and development — licenses acquired and a credit to Common shares issuable — Founders Agreement during the period ended December 31, 2015. Because the issuance of shares on February 17, 2017 occurred prior to the issuance of the December 31, 2016 financial statements, the Company recorded approximately $49,000 in research and development — licenses acquired and a credit to Common shares issuable — Founders Agreement during the period ended December 31, 2016, in connection with the stock dividend payable to holders of Class A Preferred shares, of which Fortress is the sole holder.

Fair Value Measurement

The Company follows accounting guidance on fair value measurements for financial assets and liabilities measured at fair value on a recurring basis. Under the accounting guidance, fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or a liability.

The accounting guidance requires fair value measurements be classified and disclosed in one of the following three categories:

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

Level 2: Observable inputs other than Level 1 prices, for similar assets or liabilities that are directly or indirectly observable in the marketplace.

Level 3: Unobservable inputs which are supported by little or no market activity and that are financial instruments whose values are determined using pricing models, discounted cash flow methodologies, or similar techniques, as well as instruments for which the determination of fair value requires significant judgment or estimation.

The fair value hierarchy also requires an entity to maximize the use of observable inputs and minimize the use of unobservable inputs when measuring fair value. Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

Stock-Based Compensation

The Company expenses stock-based compensation to employees over the requisite service period based on the estimated grant-date fair value of the awards. For stock-based compensation awards to non-employees, the Company measures the fair value of the non-employee awards at each reporting period prior to vesting and finally at the vesting date of the award. Changes in the estimated fair value of these non-employee awards are recognized as compensation expense in the period of change.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

The assumptions used in calculating the fair value of stock-based awards represent management's best estimates and involve inherent uncertainties and the application of management's judgment.

Fair Value Option

As permitted under the Financial Accounting Standards Board ("**FASB**"), Accounting Standards Codification ("**ASC**") 825, Financial Instruments, ("**ASC 825**"), the Company has elected the fair value option to account for its convertible notes that were issued during 2016. In accordance with ASC 825, the Company records these convertible notes at fair value with changes in fair value recorded in the Statement of Operations. As a result of applying the fair value option, direct costs and fees related to the convertible notes were recognized in earnings as incurred and were not deferred.

Valuation of Warrant Related to NSC Note — Related Party

In accordance with ASC 815, the Company classified the fair value of the warrant ("**Contingently Issuable Warrants**") that it may be obligated to issue to NSC Biotech Venture Fund I, LLC ("**NSC**"), in connection with the transfer on October 31, 2015 of $3.0 million of indebtedness to NSC, as a derivative liability as there was a potential that the Company would not have a sufficient number of authorized common shares available to settle this instrument. The Company valued these Contingently Issuable Warrants using a Black-Scholes model and used estimates for an expected dividend yield, a risk-free interest rate, and expected volatility together with management's estimate of the probability of issuance of the Contingently Issuable Warrants. At each reporting period, as long as the Contingently Issuable Warrants were potentially issuable and there was a potential for an insufficient number of authorized shares available to settle the Contingently Issuable Warrants, the Contingently Issuable Warrants should be revalued and any difference from the previous valuation date would be recognized as a change in fair value in the Company's statement of operations.

Income Taxes

The Company accounts for income taxes under ASC Topic 740, "Income Taxes ("**ASC 740**"). ASC 740 requires the recognition of deferred tax assets and liabilities for both the expected impact of differences between the financial statement and tax basis of assets and liabilities and for the expected future tax benefit to be derived from tax loss and tax credit carry forwards. ASC 740 additionally requires a valuation allowance to be established when it is more likely than not that all or a portion of deferred tax assets will not be realized.

ASC 740 also clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements and prescribes a recognition threshold and measurement process for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more-likely-than-not to be sustained upon examination by taxing authorities. ASC 740 also provides guidance on de-recognition, classification, interest and penalties, accounting in interim period, disclosure and transition. Based on the Company's evaluation, it has been concluded that there are no significant uncertain tax positions requiring recognition in the Company's financial statements. Since the Company was incorporated on February 9, 2015, the 2015 and 2016 tax years are will be the only periods subject to examination upon filing of appropriate tax returns. The Company believes that its income tax positions and deductions would be sustained on audit and does not anticipate any adjustments that would result in a material change to its financial position.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

The Company's policy for recording interest and penalties associated with audits is to record such expense as a component of income tax expense. There were no amounts accrued for penalties or interest as of or during the year ended December 31, 2016 and the period from February 9, 2015 (inception) through December 31, 2015. Management is currently unaware of any issues under review that could result in significant payments, accruals or material deviations from its position.

Licenses Acquired

In accordance with ASC 730-10-25-1, *Research and Development*, costs incurred in obtaining technology licenses are charged to research and development expense if the technology licensed has not reached commercial feasibility and has no alternative future use. The licenses purchased by the Company require substantial completion of research and development, regulatory and marketing approval efforts in order to reach commercial feasibility and has no alternative future use. Accordingly, the total purchase price of $3.0 million was reflected as research and development — licenses acquired in the Company's statement of operations for the period from February 9, 2015 (Inception) through December 31, 2015.

Net loss per Share

Loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding (excluding the impacted of unvested restricted stock) during the period. Since dividends are declared, paid and set aside among the holders of shares of common stock and Class A common stock pro-rata on an as-if-converted basis, the two-class method of computing net loss per share is not required. Diluted net loss per share does not reflect the effect of shares of common stock to be issued upon the exercise of warrants or outstanding Class A Preferred Shares, as their inclusion would be anti-dilutive. There are 50,000 warrants outstanding as of December 31, 2016 and 2015, respectively and 250,000 Class A Preferred Shares outstanding as of December 31, 2016 and none outstanding as of December 31, 2015, respectively which are excluded from the computations of net loss per share.

Comprehensive Loss

The Company has no components of other comprehensive loss, and therefore, comprehensive loss equals net loss.

Recently Issued Accounting Standards

In January 2017, the Financial Accounting Standards Board ("**FASB**") issued Accounting Standards Update ("**ASU**") No. 2017-04, *Intangibles — Goodwill and Other* (Topic 350): Simplifying the Test for Goodwill Impairment ("**ASU 2017-04**"), which eliminates the second step of the previous FASB guidance for testing goodwill for impairment and is intended to reduce cost and complexity of goodwill impairment testing. The amendments in this ASU modify the concept of impairment from the condition that exists when the carrying amount of goodwill exceeds its implied fair value to the condition that exists when the carrying amount of a reporting unit exceeds its fair value. After determining if the carrying amount of a reporting unit exceeds its fair value, the entity should take an impairment charge of the same amount to the goodwill for that reporting unit, not to exceed the total goodwill amount for that reporting unit. This eliminates the second step of calculating the implied fair value of goodwill by assigning the fair value of a reporting unit to all of its assets and liabilities as if that reporting unit had been acquired in a business combination. ASU 2017-04 is effective for annual periods beginning after December 15, 2019, including interim periods within those annual periods. Early adoption is permitted for interim or annual goodwill impairment tests performed on testing dates after January 1, 2017. The Company is currently evaluating the impact of adopting the new guidance on its financial statements.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

In January 2017, the FASB issued an ASU 2017-01, "*Business Combinations (Topic 805) Clarifying the Definition of a Business*". The amendments in this Update is to clarify the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The definition of a business affects many areas of accounting including acquisitions, disposals, goodwill, and consolidation. The guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. The Company is currently evaluating the impact of adopting this guidance.

In August 2016, the FASB issued ASU No. 2016-15,*Statement of Cash Flows — Classification of Certain Cash Receipts and Cash Payments*, which addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The standard is effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption is permitted, including adoption in an interim period. The Company is currently in the process of evaluating the impact of this new pronouncement on its statements of cash flows.

In April 2016, the FASB issued ASU No. 2016-10,*Revenue from Contracts with Customer* ("**ASU 2016-10**"). The new guidance is an update to ASC 606 and provides clarity on identifying performance obligations and licensing implementation. For public companies, ASU 2016-10 is effective for annual periods, including interim periods within those annual periods, beginning after December 15, 2016. The Company is currently evaluating the impact that ASU 2016-10 will have on its financial statements.

In March 2016, the FASB issued ASU No. 2016-09*Compensation-Stock Compensation (Topic 718), Improvements to Employee Share-Based Payment Accounting* ("**ASU 2016-09**"). Under ASU 2016-09, companies will no longer record excess tax benefits and certain tax deficiencies in additional paid-in capital ("**APIC**"). Instead, they will record all excess tax benefits and tax deficiencies as income tax expense or benefit in the income statement and the APIC pools will be eliminated. In addition, ASU 2016-09 eliminates the requirement that excess tax benefits be realized before companies can recognize them. ASU 2016-09 also requires companies to present excess tax benefits as an operating activity on the statement of cash flows rather than as a financing activity. Furthermore, ASU 2016-09 will increase the amount an employer can withhold to cover income taxes on awards and still qualify for the exception to liability classification for shares used to satisfy the employer's statutory income tax withholding obligation. An employer with a statutory income tax withholding obligation will now be allowed to withhold shares with a fair value up to the amount of taxes owed using the maximum statutory tax rate in the employee's applicable jurisdiction(s). ASU 2016-09 requires a company to classify the cash paid to a tax authority when shares are withheld to satisfy its statutory income tax withholding obligation as a financing activity on the statement of cash flows. Under current GAAP, it was not specified how these cash flows should be classified. In addition, companies will now have to elect whether to account for forfeitures on share-based payments by (1) recognizing forfeitures of awards as they occur or (2) estimating the number of awards expected to be forfeited and adjusting the estimate when it is likely to change, as is currently required. The Amendments of this ASU are effective for reporting periods beginning after December 15, 2016, with early adoption permitted but all of the guidance must be adopted in the same period. The Company is currently assessing the impact the adoption of ASU 2016-09 will have on its financial statements.

In February 2016, the FASB issued ASU No. 2016-02,*Leases (Topic 842)* ("**ASU 2016-02**") which supersedes FASB Accounting Standards Codification ("**ASC**") Topic 840, *Leases (Topic 840)* and provides principles for the recognition, measurement, presentation and disclosure of leases for

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

both lessees and lessors. The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than twelve months regardless of classification. Leases with a term of twelve months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for annual and interim periods beginning after December 15, 2018, with early adoption permitted upon issuance. The Company is currently evaluating the method of adoption and the impact of adopting ASU 2016-02 on its financial statements. When adopted, the Company does not expect this guidance to have a material impact on its financial statements.

In January 2016, the FASB issued ASU No. 2016-01,*Recognition and Measurement of Financial Assets and Financial Liabilities* ("**ASU 2016-01**") . ASU 2016-01 requires equity investments to be measured at fair value with changes in fair value recognized in net income; simplifies the impairment assessment of equity investments without readily determinable fair values by requiring a qualitative assessment to identify impairment; eliminates the requirement for public business entities to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet; requires public business entities to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes; requires an entity to present separately in other comprehensive income the portion of the total change in the fair value of a liability resulting from a change in the instrument-specific credit risk when the entity has elected to measure the liability at fair value in accordance with the fair value option for financial instruments; requires separate presentation of financial assets and financial liabilities by measurement category and form of financial assets on the balance sheet or the accompanying notes to the financial statements and clarifies that an entity should evaluate the need for a valuation allowance on a deferred tax asset related to available-for-sale securities in combination with the entity's other deferred tax assets. ASU 2016-01 is effective for financial statements issued for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. The Company is currently evaluating the impact that ASU 2016-01 will have on its balance sheet or financial statement disclosures. When adopted, the Company does not expect this guidance to have a material impact on its financial statements.

Recently Adopted Accounting Pronouncements

As of October 2015, the Company adopted a sequencing policy whereby all future instruments may be classified as a derivative liability with the exception of instruments related to share-based compensation issued to employees or directors.

In April 2015, the Financial Accounting and Reporting Standards ("**FASB**") issued Accounting Standard Update ("**ASU**") 2015-03, Simplifying the Presentation of Debt Issuance Costs ("**ASU 2015-03**"), which requires debt issuance costs to be presented in the balance sheet as a direct deduction from the carrying value of the associated debt liability, consistent with the presentation of a debt discount. ASU 2015-03 is effective for the interim and annual periods ending after December 15, 2015. The Company adopted ASU 2015-03 on March 31, 2015. The adoption did not have an impact on the financial statements and related disclosures.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 2 — Significant Accounting Policies – (continued)

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern ("**ASU No. 2014-15**") that will require management to evaluate whether there are conditions and events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the financial statements are issued on both an interim and annual basis. Management will be required to provide certain footnote disclosures if it concludes that substantial doubt exists or when its plans alleviate substantial doubt about the Company's ability to continue as a going concern. We adopted ASU 2014-15 in the fourth quarter of 2016, and its adoption did not have a material impact on our financial statements.

Note 3 — Allocation

The expense allocations to Avenue, which represent Lucy Lu's executive compensation, have been paid by Fortress and allocated by the Company between Avenue and Fortress based on time spent on Avenue projects versus time spent on Fortress projects. The allocations were based on assumptions that management believes are reasonable; however, these allocations are not necessarily indicative of the costs and expenses that would have resulted if Avenue had been operating as a stand-alone entity. For the period from February 9, 2015 (Inception) through December 31, 2015, the allocated expenses related to Lucy Lu were approximately $95,000 and were recorded 50% to research and development and 50% to general and administration expenses. For the year ended December 31, 2016, the allocated expenses related to Lucy Lu were approximately $336,000, of which $136,000 represent a 2016 bonus payable and were recorded 50% to research and development and 50% to general and administration expenses.

Note 4 — License Agreement

Effective as of February 17, 2015, Fortress transferred the Revogenex license and all other rights and obligations under the License Agreement to Avenue, pursuant to the terms of the Founders Agreement. In connection with the terms of the License Agreement, Fortress purchased an exclusive license to IV Tramadol for the U.S. market from Revogenex, a privately held company in Dublin, Ireland. Tramadol is a centrally acting synthetic opioid analgesic for moderate to moderately severe pain and is available as immediate release or extended-release tablets in the United States. Fortress made an upfront payment of $2.0 million to Revogenex upon execution of the exclusive license, and on June 17, 2015, Fortress paid an additional $1.0 million to Revogenex after receiving all the assets specified in the agreement. The $3.0 million cumulative payment has been included in research and development-licenses acquired on the statements of operations. In addition, under the terms of the agreement, Revogenex is eligible to receive additional milestone payments upon the achievement of certain development milestones, as well as royalty payments for sales of the product.

Additionally, on March 10, 2015, the Company entered into a consulting agreement with the CEO of Revogenex (the "**Consultant**") to provide consulting services to the Company. Under the terms of the agreement, the Company will pay $25,000 per calendar quarter to the Consultant throughout the initial one year term of the agreement. Either party upon 30-days written notice can terminate the agreement. From March 10, 2015 through December 31, 2015, the Company paid the Consultant approximately $83,000. For the year ended December 31, 2016, the Company had expenses related to the Consultant of approximately $16,000.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 5 — Related Party Agreements

Founders Agreement and Management Services Agreement with Fortress

Effective as of February 17, 2015, Fortress and the Company entered into a Founders Agreement pursuant to which Fortress assigned to Avenue all of its right and interest under Fortress' license agreement with Revogenex for IV Tramadol. As consideration for the Founders Agreement, the Company assumed $3.0 million in debt that Fortress accumulated under the NSC Note (See Note 6) for the IV Tramadol license, of which $2.0 million represents the initial payment in February 2015 and $1.0 million the payment made in June 2015. As additional consideration for the transfer of rights under the Founders Agreement, the Company will also: (i) issue annually to Fortress, on the anniversary date of the Founders Agreement, shares of common stock equal to 2.50% of the fully-diluted outstanding equity of Avenue at the time of issuance; (ii) pay an equity fee in shares of common stock, payable within five (5) business days of the closing of any equity or debt financing for Avenue or any of its respective subsidiaries that occurs after the effective date of the Founders Agreement and ending on the date when Fortress no longer has majority voting control in Avenue's voting equity, equal to two and one half percent (2.50%) of the gross amount of any such equity or debt financing; and (iii) pay a cash fee equal to four and one half percent (4.5%) of our annual net sales, payable on an annual basis, within ninety (90) days of the end of each calendar year. In the event of a change in control (as it is defined in the Founders Agreement), we will pay a one-time change in control fee equal to five (5x) times the product of (i) monthly net sales for the twelve (12) months immediately preceding the change in control and (ii) four and one-half percent (4.5%).

On September 13, 2016, the Company entered into an Amended and Restated the Founders Agreement ("**A&R Founders Agreement**") with Fortress. The A&R Founders Agreement eliminated the Annual Equity Fee in connection with the original agreement and added a term of 15 years, which upon expiration automatically renews for successive one-year periods unless terminated by Fortress or a Change in Control occurs. Concurrently with the A&R Founders Agreement, the Company entered into an Exchange Agreement whereby the Company exchanged Fortress's 7.0 million Class A common shares for approximately 7.5 million common shares and 250,000 Class A Preferred shares. In connection with the issuance of Class A Preferred shares, Fortress will receive an annual stock dividend (see below).

Effective as of February 17, 2015, the Company entered into a Management Services Agreement (the "**MSA**") with Fortress and each of the Company's current directors and officers who are directors or officers of Fortress to provide services to the Company pursuant to the terms of the MSA. Pursuant to the terms of the MSA, for a period of five (5) years, Fortress will render advisory and consulting services to the Company. Services provided under the MSA may include, without limitation, (i) advice and assistance concerning any and all aspects of our operations, clinical trials, financial planning and strategic transactions and financings and (ii) conducting relations on behalf of our Company with accountants, attorneys, financial advisors and other professionals (collectively, the "**Services**"). The Company is obligated to utilize clinical research services, medical education, communication and marketing services and investor relations/public relation services of companies or individuals designated by Fortress, provided those services are offered at market prices. However, the Company is not obligated to take or act upon any advice rendered from Fortress and Fortress shall not be liable for any of our actions or inactions based upon their advice. Fortress and its affiliates, including all members of the Company's Board of Directors, have been contractually exempt from fiduciary duties to the Company relating to corporate opportunities. In consideration for the Services, the Company will pay Fortress an annual consulting fee of $0.5 million (the "**Annual Consulting Fee**"), payable in advance in equal quarterly installments on the first business day of each calendar quarter in each year, provided, however, that such Annual Consulting Fee shall be increased to $1.0 million for each calendar year

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 5 — Related Party Agreements – (continued)

in which the Company has net assets in excess of $100 million at the beginning of the calendar year. For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) to December 31, 2015, the Company recognized approximately $500,000 and $417,000, respectively, in expense on the Statement of Operations related to the MSA.

Issuance of Common Shares to Fortress

In connection with the Founders Agreement with Fortress, for the period ended December 31, 2015, the Company recorded an annual equity fee of $40,000 representing the 228,750 shares of our common stock at $0.176 per share. The annual equity fee represents 2.5% of the outstanding shares of the Company, issuable on the anniversary date of the Founders Agreement. As such, on February 17, 2016, the shares were issued. On September 13, 2016, in connection with the Amended and Restated Founders Agreement, the Equity Fee was eliminated.

For the period ended December 31, 2016, in connection with the 250,000 Class A Preferred shares, the Company recorded an expense of $49,000, representing the expense related to the Preferred A stock dividend. The expense is related to the 250,595 common shares issuable to Fortress on the anniversary date of the Amended and Restated Founders Agreement, representing 2.5% of the outstanding shares of the Company at December 31, 2016, at $0.194 per share or $49,000.

For the year ended December 31, 2016, and from inception to December 31, 2015, the Company recorded expenses of $49,000 and $40,000 in research and development licenses acquired.

Fortress Note

Effective March 15, 2015, the Company and Fortress entered into a future advance promissory note (the '**Fortress Note**"), in which Fortress agreed to provide a working capital line of credit until the Company has a third party financing. Interest on the Fortress Note is being accrued at 8% per annum and shall be payable to Fortress on the day after the end of each calendar quarter following the first third party financing. All principal and accrued interest under the Fortress Note is payable on demand following the first third party financing. This Fortress Note can be pre-paid at any time in cash or through the assumption of Fortress' indebtedness NSC or other similar indebtedness.

As of December 31, 2016, the Fortress Note totaled approximately $2.8 million. For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) to December 31, 2015, the Company had interest expense related to the Fortress Note of $178,000 and $164,000, respectively.

Consulting Agreement with Chord Advisors, LLC ("Chord")

On June 12, 2015, the Company entered into a full-service consulting agreement with Chord to provide advisory accounting services to the Company. Under the terms of the agreement, the Company will pay Chord five thousand dollars ($5,000) per month prior to becoming a public company and seven thousand five hundred dollars ($7,500) per month thereafter to perform back office accounting functions, accounting analysis and financial reporting. Either party upon 30-days written notice can terminate the agreement. In addition to these services, Mr. Horin, a Managing Partner of Chord, serves as the Company's Interim Chief Financial Officer. Chord also provides advisory accounting services to Fortress under a separate agreement.

For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) to December 31, 2015, the Company recognized approximately $50,000 and $35,000, respectively, in expense on the Statement of Operations.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 5 — Related Party Agreements – (continued)

NSC Note and Financings

In September 2016, Fortress acquired through a tender offer 56.6% of National Holdings, Inc. ("**National**" or "**NHLD**"). The Company holds a $3.0 million note in favor of NSC Biotech Venture Fund I, LLC for which National Securities, Inc. ("**NSC**"), a subsidiary of National, received a 10% placement fee upon issuance of the Note to Fortress. In addition, upon the completion of a third party raise of five times the NSC Note, the Company will issue a warrant to NSC as the placement agent equal to 25% of the outstanding debt. At December 31, 2016 and 2015 the Company recorded a derivate liability of $302,000 and $114,000 respectively on the Company's balance sheet.

Note 6 — Notes Payable

NSC Note

In February 2015, Fortress closed a private placement of a promissory note for $10 million in favor of NSC Biotech Venture Fund I, LLC, (the "**NSC Note**"). Fortress used the proceeds from the NSC Note to acquire medical technologies and products. The note matures in 36 months, provided that during the first 24 months Fortress can extend the maturity date by six months. No principal amount will be due for the first 24 months (or the first 30 months if the maturity date is extended). Thereafter, the note will be repaid at the rate of 1/12 of the principal amount per month for a period of 12 months. Interest on the note is 8% payable quarterly during the first 24 months (or the first 30 months if the note is extended) and monthly during the last 12 months. National Securities Corporation ("**NSC**"), a wholly owned subsidiary of National Holdings, Inc., acted as the sole placement agent for the NSC Note. In January 2017, the Company notified NSC Biotech Venture Fund I, LLC, of its election to extend the maturity date to September 30, 2018.

The NSC Note, was amended and restated on July 29, 2015, to provide that any time a Fortress Company receives from Fortress any proceeds from the NSC Note, Fortress may, in its sole discretion, cause the Fortress Company to issue to NSC Biotech Venture Fund I, LLC a new promissory note (the "**Amended NSC Note**") on identical terms as the NSC Note (giving effect to the passage of time with respect to maturity). The Amended NSC Note will equal the dollar amount of the Fortress Company's share of the NSC Note and reduce the Fortress' obligations under the NSC Note by such amount. Fortress will guarantee the Amended NSC Note until the Company either completes an initial public offering of its securities or raises sufficient equity capital so that it has cash equal to five times the Amended NSC Note.

If the Company has an initial public offering and raises sufficient equity capital so that it has cash equal to five times the amount of the portion of the proceeds of the NSC Note transferred to it, then NSC will receive a warrant to purchase the Company's stock equal to 25% of the outstanding note divided by the lowest price the Company sells its equity in its first third party financing. The warrants issued will have a term of 10 years and an exercise price equal to the par value of the Company's common stock.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 6 — Notes Payable – (continued)

As of December 31, 2016, the Company's Amended NSC Note totaled $3.0 million, with a debt discount related to the Company's pro rata share of Fortress' debt issuance costs of approximately $174,000. For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) to December 31, 2015, the Company recorded costs of approximately $123,000 and $73,000, respectively, related to the amortization of the debt discount and approximately $241,000, of which $14,000 is payable to a related party and $145,000 of which $3,500 is payable to a related party, respectively, of interest expense at 8%, both recorded in interest expense on the Statement of Operations. The effective interest rate of the NSC Note approximates 13.1%. The warrant contingently issuable in connection with NSC Note in the amount of approximately $114,000 was recorded as a debt discount based on its fair value (see Note 9). The following table summarizes NSC Note activities as of December 31, 2015 (in thousands).

	Note Payable	Discount	Note Payable, Net
February 9, 2015 balance	$ —	$ —	$ —
Proceeds from issuance of NSC Note	3,000	(256)	2,744
Amortization of debt discount	—	73	73
Derivative warrant liability	—	(114)	(114)
December 31, 2015 balance	$ 3,000	$ (297)	$ 2,703
Amortization of debt discount	—	123	123
December 31, 2016 balance	$ 3,000	$ (174)	$ 2,826

Fortress Note

As of December 31, 2016, the Company's Note from Fortress used to fund it working capital totaled $2.8 million. The note accrues interest at 8% (see Note 5). For the year ended December 31, 2016 and the period from February 9, 2015 (Inception) to December 31, 2015, the Company recognized approximately $178,000 and $168,000, respectively, in expense on the Statement of Operations.

Westpark Convertible Note

On December 30, 2016, Avenue held a closing of the sale of convertible promissory notes. Avenue sold three convertible promissory notes to investors for an aggregate of $200,000. The notes have an initial term of 18 months, which can be extended at the option of the holder, on one or more occasions, for up to 180 days and accrue simple interest at the rate of 5% per annum for the first 12 months and 8% per annum simple interest thereafter. The notes are guaranteed by Fortress. The outstanding principal and interest of the notes automatically converts into the type of equity securities sold by Avenue in the next sale of equity securities in which Avenue realizes aggregate gross cash proceeds of at least $10.0 million (before commissions or other expenses and excluding conversion of the notes) at a conversion price equal to the lesser of (a) the lowest price per share at which equity securities of Avenue are sold in such sale less a 33% discount and (b) a per share price based on a pre-offering valuation of $30.0 million divided by the number of common shares outstanding on a fully-diluted basis. The outstanding principal and interest of the notes may be converted at the option of the holder in any sale of equity securities that does not meet the $10.0 million threshold for automatic conversion using the same methodology. The notes also automatically convert upon a "Sale" of Avenue, defined as (a) a transaction or series of related transactions where one or more non-affiliates acquires (i) capital stock of Avenue or any surviving successor entity possessing the voting power to elect a majority of the board of directors or (ii) a majority of the outstanding capital stock of Avenue or the surviving successor entity (b) the sale, lease or other disposition of all or substantially all of Avenue's assets or any other transaction resulting in substantially all of Avenue's assets being converted into securities of another entity or

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 6 — Notes Payable – (continued)

cash. Upon a Sale of Avenue, the outstanding principal and interest of the notes automatically converts into common shares at a price equal to the lesser of (a) a discount to the price per share being paid in the Sale of Avenue equal to 33% or (b) the quotient resulting from dividing (x) $30.0 million by (y) the fully-diluted common stock of Avenue outstanding immediately prior to the Sale of Avenue (excluding the notes).

In the closing, Avenue realized net proceeds of $142,000 after paying WestPark Capital, Inc., the placement agent, placement agent fees of $30,000 and escrow fees of $4,000 and paying approximately $14,000 in legal fees. Additionally, WestPark received a warrant ("**Avenue Warrant**") to purchase the number of shares of Avenue's common stock equal to $10,000 divided by the price per share at which any note sold to investors first converts into Avenue's common stock. The Avenue Warrant has a ten-year term and has a per share exercise price equal to the price per share at which any note sold to investors first converts into Avenue's common stock.

The fair value of these convertible notes amounted to $200,000.

Due to the complexity and number of embedded features within each convertible note, and as permitted under accounting guidance, the Company elected to account for the convertible notes and all the embedded features (collectively, the "hybrid instrument") under the fair value option.

Note 7 — Commitments and Contingencies

Leases

The Company is not a party to any leases for office space or equipment.

Litigation

The Company recognizes a liability for a contingency when it is probable that liability has been incurred and when the amount of loss can be reasonably estimated. When a range of probable loss can be estimated, the Company accrues the most likely amount of such loss, and if such amount is not determinable, then the Company accrues the minimum of the range of probable loss. As of December 31, 2016, there was no litigation against the Company.

Note 8 — Stockholders' Deficit

Class A Preferred Shares

Pursuant to the Company's Second Amended and Restated Certificate of Incorporation, filed September 13, 2016, Class A Common Stock was eliminated and 2,000,000 shares are Preferred Stock were authorized, of which 250,000 have been designated as Class A Preferred Stock and the remainder are undesignated preferred stock. The Class A Preferred Stock, with a par value of $0.0001 per share, is identical to undesignated Common Stock other than as to voting rights, conversion rights, and the PIK Dividend right (as described below). The undesignated Preferred Stock may be issued from time to time in one or more series. The Company's Board of Directors is authorized to determine or alter the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions, if any), the redemption price or prices, the liquidation preferences and other designations, powers, preferences and relative, participating, optional or other special rights, if any, and the qualifications, limitations and restrictions granted to or imposed upon any wholly unissued series of Preferred Stock, and to fix the number of shares of any series of Preferred Stock (but not below the number of shares of any such series then outstanding).

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 8 — Stockholders' Deficit – (continued)

The holders of the outstanding shares of Class A Preferred Stock shall receive on each February 17 (each a "**PIK Dividend Payment Date**") after the original issuance date of the Class A Preferred Stock until the date all outstanding Class A Preferred Stock is converted into Common Stock or redeemed (and the purchase price is paid in full), pro rata per share dividends paid in additional fully paid and nonassessable shares of Common Stock (such dividend being herein called "**PIK Dividends**") such that the aggregate number of shares of Common Stock issued pursuant to such PIK Dividend is equal to two and one-half percent (2.5%) of the Corporation's fully-diluted outstanding capitalization on the date that is one (1) business day prior to any PIK Dividend Payment Date ("**PIK Record Date**"). In the event the Class A Preferred Stock converts into Common Stock, the holders shall receive all PIK Dividends accrued through the date of such conversion. No dividend or other distribution shall be paid, or declared and set apart for payment (other than dividends payable solely in capital stock on the capital stock of the Company) on the shares of Common Stock until all PIK Dividends on the Class A Preferred Stock shall have been paid or declared and set apart for payment. All dividends are non-cumulative.

On any matter presented to the stockholders of the Company for their action or consideration at any meeting of stockholders of the Company (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Class A Preferred Stock shall be entitled to cast for each share of Class A Preferred Stock held by such holder as of the record date for determining stockholders entitled to vote on such matter, the number of votes that is equal to one and one-tenth (1.1) times a fraction, the numerator of which is the sum of (A) the number of shares of outstanding Common Stock and (B) the whole shares of Common Stock in to which the shares of outstanding Class A Common Stock and the Class A Preferred Stock are convertible, and the denominator of which is number of shares of outstanding Class A Preferred Stock (the "**Class A Preferred Stock Ratio**"). Thus, the Class A Preferred Stock will at all times constitute a voting majority.

Each share of Class A Preferred Stock is convertible, at the option of the holder, into one fully paid and nonassessable share of Common Stock (the "**Conversion Ratio**"), subject to certain adjustments. If the Company, at any time effects a subdivision or combination of the outstanding Common Stock (by any stock split, stock dividend, recapitalization, reverse stock split or otherwise), the applicable Conversion Ratio in effect immediately before that subdivision is proportionately decreased or increased, as applicable, so that the number of shares of Common Stock issuable on conversion of each share of Class A Preferred Stock shall be increased or decreased, a applicable, in proportion to such increase or decrease in the aggregate number of shares of Common Stock outstanding. Additionally, if any reorganization, recapitalization, reclassification, consolidation or merger involving the Company occurs in which the Common Stock (but not the Class A Preferred Stock) is converted into or exchanged for securities, cash or other property, then each share of Class A Preferred Stock becomes convertible into the kind and amount of securities, cash or other property which a holder of the number of shares of Common Stock of the Company issuable upon conversion of one share of the Class A Preferred Stock immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction.

Common Stock

The Company was authorized to issue 50,000,000 common shares with a par value of $0.0001 per share, of which, 15,000,000 shares were designated as "Class A Common Stock". Fortress subscribed for 7,000,000 of the Class A Common Stock and 1,000,000 shares of the Common Stock. Fortress paid the par value of $800. Dividends are to be distributed pro-rata to the Class A Common Stock and common stock holders. The holders of common stock are entitled to one vote per share of common stock held. The Class A Common Stock holders are entitled to a number of votes equal to 1.1 times a fraction the numerator of which is the sum of (A) the shares of

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 8 — Stockholders' Deficit – (continued)

outstanding common stock and (B) the whole shares of common stock into which the shares of outstanding Class A Common Stock are convertible and the denominator of which is the number of shares of Class A Common Stock. Each share of Class A Common Stock shall be convertible, at the option of the holder thereof, into one (1) full paid and non-assessable share of common stock subject to adjustment for stock splits and combinations.

Pursuant to the Founders Agreement, on February 17, 2016, the Company issued 228,750 shares of common stock to Fortress, which equaled to 2.5% of the fully diluted outstanding equity of Avenue at the time of issuance for the annual equity fee. The Company recorded an expense of approximately $40,000, in research and development licenses-acquired related to this stock grant during the period ended December 31, 2015.

On September 13, 2016, the Company entered into an Amended and Restated the Founders Agreement ("**A&R Founders Agreement**") with Fortress. The A&R Founders Agreement eliminated the Annual Equity Fee in connection with the original agreement and added a term of 15 years, which upon expiration automatically renews for successive one-year periods unless terminated by Fortress or a Change in Control occurs. Concurrently with the A&R Founders Agreement the Company entered into an Exchange Agreement whereby the Company exchanged Fortress' 7.0 million Class A common shares for 7.4 million common shares and 250,000 Class A Preferred shares. The Company also eliminated its Class A Common Stock in July 2016, in connection with the transactions above.

On September 15, 2016, the Company retired the 100,000 shares of restricted stock issued to a consultant in connection with a May 2015 subscription agreement.

Stock Grants

On May 13, 2015, the Company granted 100,000 shares to a consultant, an employee of Fortress. These shares were granted in connection with services provided to the Company by a consultant. These shares are vested. The stock price was determined utilizing a discounted cash flow model prepared by the Company to determine the weighted market value of invested capital, discounted by a lack of marketability of 44.8%, weighted average cost of capital of 30%, and net of debt utilized, resulting in a value of $0.146 per share.

On May 13, 2015, the Company granted 50,000 shares to a consultant, also an employee of TG Therapeutics, Inc., of which Mr. Michael Weiss is Executive Chairmen, Interim President and Chief Executive Officer. These shares were granted in connection with services provided to the Company by the consultant. These shares are immediately vested and have a value of $0.146 per share in accordance with a valuation performed by the Company.

On June 10, 2015, the Company granted 1,000,000 shares to Dr. Lu, the Company's Interim President and Chief Executive Officer. Half of these shares cliff vest in four tranches over 4 years and the other half vest based upon achievement of performance milestones. The shares have a value of $0.146 per share in accordance with a valuation performed by the Company.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 8 — Stockholders' Deficit – (continued)

The following table summarizes restricted stock award activity for the period from February 9, 2015 (Inception) through December 31, 2015 and the year ended December 31, 2016.

	Number of Units	Weighted Average Grant Day Fair Value
Nonvested at February 9, 2015 (Inception)	—	$ —
Granted	1,150,000	0.15
Vested	(150,000)	0.15
Nonvested at December 31, 2015	1,000,000	$ 0.15
No activity	—	—
Nonvested at December 31, 2016	1,000,000	$ 0.15

For the period from February 9, 2015 (Inception) through December 31, 2015, stock-based compensation expenses associated with the amortization of restricted stock award for employees and non-employees were approximately $29,000 and $22,000, respectively.

For the year ended December 31, 2016, stock-based compensation expenses associated with the amortization of restricted stock award for employees and non-employees were approximately $28,000 and $nil, respectively.

At December 31, 2016, the Company had unrecognized stock-based compensation expense related to restricted stock awards of $24,000, which is expected to be recognized over the remaining weighted-average vesting period of 1.63 years.

Note 9 — Fair Value Measurement

Financial instruments measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. At December 31, 2016 and 2015, the warrant balance of approximately $314,000 and $114,000, respectively, were classified as Level 3 instruments.

The following table sets forth the changes in the estimated fair value for our Level 3 classified derivative warrant liability ($in thousands):

	(1) NSC Contingently Issuable Warrants	Westpark Contingently Issuable Warrants	Total
Fair value, February 9, 2015 (Inception)	$ —	$ —	$ —
Issuance of derivative warrant liabilities	114	—	114
Fair value, December 31, 2015	114	—	114
Issuable derivative warrant liabilities	—	12	12
Change in fair value	188	—	188
Fair value, December 31, 2016	$ 302	$ 12	$ 314

(1) NSC, as the placement agent, is a Related Party.

If the Company has an initial public offering and raises sufficient equity capital so that it has cash equal to five times the amount of the portion of the proceeds of the NSC Note transferred to it, then NSC will receive a warrant to purchase the Company's stock equal to 25% of the outstanding note divided by the lowest price the Company sells its equity in its first third party financing. The warrants issued will have a term of 10 years and an exercise price equal to the par value of the

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 9 — Fair Value Measurement – (continued)

Company's common stock. In accordance with ASC 815 — "*Derivatives and Hedging (Topic 815)*", the Company classified the fair value of the warrant that maybe granted in connection with the NSC Note transferred to the Company on December 31, 2016 as a derivative liability as there was a potential that the Company would not have a sufficient number of authorized common shares available to settle this instrument. The Company valued this warrant using a Black-Scholes model and estimates for an expected dividend yield, a risk-free interest rate, and expected volatility together with management's estimate of the probability of issuance of the warrant. Management's estimate of probability of issuance of the warrant was based upon market participant data related to levels of common stock financings in comparison to market capitalizations of comparable companies. At each reporting period, as long as the warrant was potentially issuable and there was a potential for an insufficient number of authorized shares available to settle the warrant, the warrant will be revalued and any difference from the previous valuation date will be recognized as a change in fair value in the Company's statement of operations.

The fair value of the NSC Contingently Issuable Warrants was determined at December 31, 2016 for approximately $302,000 by applying management's estimate of the probability of issuance of the Contingently Issuable Warrants together with the Black-Scholes option pricing model with the following key assumptions:

	December 31, 2016	December 31, 2015
Risk-free interest rate	2.45%	2.27%
Expected dividend yield	—	—
Expected term in years	10.00	10.00
Expected volatility	83%	83%
Probability of issuance of the warrant	50%	25%

The fair value of Westpark warrant liability was measured at fair value using a Monte Carlo simulation valuation methodology. A summary of the weighted average (in aggregate) significant unobservable inputs (level 3 inputs) used in measuring the Company's warrant liabilities that are categorized within Level 3 of the fair value hierarchy for the year ended December 31, 2016 is as follows:

	December 31, 2016
Risk-free interest rate	2.45%
Expected dividend yield	—
Expected term in years	10.00
Expected volatility	87%

The following table sets forth the changes in the estimated fair value for our Level 3 classified convertible notes payable ($in thousands):

	Westpark Convertible Notes
Fair value, December 31, 2015	$ —
Additions	200
Change in fair value	—
Fair value, December 31, 2016	$ 200

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 10 — Income Taxes

For financial reporting purposes, the Company calculated income tax provision and deferred income tax balances as if it was a separate entity and had filed its own separate tax return under Sub-Chapter C of the Internal Revenue Code.

A reconciliation of the statutory U.S. federal rate to the Company's effective tax rate is as follows:

	For the years ended December 31,	
	2016	2015
Statutory federal income tax rate	35%	35%
State taxes, net of federal tax benefit	4%	5%
Rate change	(1)%	—
Change in valuation allowance	(38)%	(40)%
Income taxes provision (benefit)	—	—

The components of the net deferred tax asset as of December 31, 2016 and 2015 are the following (in thousands):

	As of December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carryovers	$ 2,080	$ 887
Change in warrant liabilities	73	—
Amortization of license	1,064	1,136
Accruals and reserves	78	95
Tax credits	33	19
Total deferred tax assets	3,328	2,137
Less valuation allowance	(3,318)	(2,090)
Stock compensation and other	(10)	(47)
Deferred tax asset, net of valuation allowance	$ —	$ —

The Company has determined, based upon available evidence, that it is more likely than not that the net deferred tax asset will not be realized and, accordingly, has provided a full valuation allowance against it. A valuation allowance of approximately $3.3 million and $2.1 million was recorded for the period ended December 31, 2016 and 2015, respectively.

As of December 31, 2016, the Company had federal and state net operating loss carryforwards of approximately $5.3 million and $4.1 million, respectively. The federal and state net operating loss carryforwards will begin to expire, if not utilized, by 2035 and 2025, respectively. Utilization of the net operating loss carryforward may be subject to an annual limitation due to the ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended and similar state provisions.

The Company is included in the consolidated income tax returns of Fortress Biotech, Inc. and Subsidiaries. The Company's federal and state net operating loss carryforwards may be utilized to offset income of other members included in the consolidated income tax returns for which the Company may be compensated pursuant to outstanding tax-sharing agreements.

AVENUE THERAPEUTICS, INC

Notes to Financial Statements

Note 10 — Income Taxes – (continued)

There are no significant matters determined to be unrecognized tax benefits taken or expected to be taken in a tax return, in accordance with 740 "Income Taxes" ("**ASC 740**"), which clarifies the accounting for uncertainty in income taxes recognized in the financial statements, that have been recorded on the Company's financial statements for the period ended December 31, 2016. The Company does not anticipate a material change to unrecognized tax benefits in the next twelve months.

Additionally, ASC 740 provides guidance on the recognition of interest and penalties related to income taxes. There were no interest or penalties related to income taxes that have been accrued or recognized as of and for the period ended December 31, 2016.

The federal and state tax returns for the period ended December 31, 2015 are currently open for examination under the applicable federal and state income tax statues of limitations.

TABLE OF CONTENTS

shares
Common Stock

Avenue Therapeutics, Inc.

PROSPECTUS

, 2017

Sole Book-Running Manager

RAYMOND JAMES

Co-Manager

NATIONAL SECURITIES CORPORATION

Through and including , 2017 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution

	Amount to Be Paid
SEC Registration fee	$
Legal fees and expenses	$ *
FINRA filing fee	$ *
NASDAQ listing fee	$ *
Accounting fees and expenses	$ *
Printing expenses	$ *
Transfer agent fees and expenses	$ *
Miscellaneous	$ *
Total	$

Each of the amounts set forth above, other than the registration fee, is an estimate.

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers

We have adopted provisions in our Second Amended and Restated Certificate of Incorporation that limit the liability of our directors for monetary damages for breach of their fiduciary duties, except for liability that cannot be eliminated under the DGCL. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except liability for any of the following:

- any breach of their duty of loyalty to the corporation or the stockholder;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the DGCL; or
- any transaction from which the director derived an improper personal benefit.

This limitation of liability does not apply to liabilities arising under the federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our Second Amended and Restated Certificate of Incorporation and our Bylaws also provide that we will indemnify our directors and executive officers and may indemnify our other officers and employees and other agents to the fullest extent permitted by law. We believe that indemnification under our Bylaws covers at least negligence and gross negligence on the part of indemnified parties. Our Bylaws also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in this capacity, regardless of whether our Bylaws would permit indemnification. We have secured such insurance.

Item 15. Recent Sales of Unregistered Securities

On December 30, 2016, we held a closing of the sale of convertible promissory notes. We sold three convertible promissory notes to investors for an aggregate of $0.2 million. The notes have an initial term of 18 months, which can be extended at the option of the holder, on one or more occasions, for up to 180 days and accrue simple interest at the rate of 5% per annum for the first 12 months and 8% per annum simple interest thereafter. The notes are guaranteed by Fortress. The outstanding principal and interest of the notes automatically converts into the type of equity

securities sold by us in the next sale of equity securities in which we realize aggregate gross cash proceeds of at least $10.0 million (before commissions or other expenses and excluding conversion of the notes) at a conversion price equal to the lesser of (a) the lowest price per share at which equity securities of Avenue are sold in such sale less a 33% discount and (b) a per share price based on a pre-offering valuation of $30.0 million divided by the number of common shares outstanding on a fully-diluted basis. The outstanding principal and interest of the notes may be converted at the option of the holder in any sale of equity securities that does not meet the $10.0 million threshold for automatic conversion using the same methodology. The notes also automatically convert upon a "Sale" of us, defined as (a) a transaction or series of related transactions where one or more non-affiliates acquires (i) capital stock of us or any surviving successor entity possessing the voting power to elect a majority of the board of directors or (ii) a majority of the outstanding capital stock of us or the surviving successor entity (b) the sale, lease or other disposition of all or substantially all of our assets or any other transaction resulting in substantially all of our assets being converted into securities of another entity or cash. Upon a Sale of us, the outstanding principal and interest of the notes automatically converts into common shares at a price equal to the lesser of (a) a discount to the price per share being paid in the Sale of us equal to 33% or (b) the quotient resulting from dividing (x) $30.0 million by (y) our fully-diluted common stock outstanding immediately prior to the Sale (excluding the notes).

In the closing, we realized net proceeds of $142,000 after paying WestPark Capital, Inc., the placement agent, placement agent fees of $30,000 and escrow fees of $4,000. Additionally, WestPark received a warrant ("Avenue Warrant") to purchase the number of shares of our common stock equal to $10,000 divided by the price per share at which any note sold to investors first converts into our common stock. The Avenue Warrant has a ten-year term and has a per share exercise price equal to the price per share at which any note sold to investors first converts into our common stock.

Item 16. Exhibits and Financial Statement Schedules

(a) Exhibits

The exhibits to the registration statement are listed in the Exhibit Index to this registration statement and are incorporated herein by reference.

(b) Financial Statements Schedules:

Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto included elsewhere in this registration statement.

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes to provide to the underwriter at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

(b) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer, or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

(c) The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

SIGNATURES

Pursuant to the requirements of Section 12 of the Securities Exchange Act of 1934, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized in the City of New York, State of New York, on this 27th day of March, 2017.

Avenue Therapeutics, Inc.

By: /s/ Lucy Lu, M.D.
Name: Lucy Lu, M.D.
Title: Interim President, Chief Executive Officer and Director

March 27, 2017

POWER OF ATTORNEY

We, the undersigned directors and/or executive officers of Avenue Therapeutics, Inc., hereby severally constitute and appoint Lucy Lu, M.D., acting singly, his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her in any and all capacities, to sign this registration statement and to file the same, with all exhibits thereto and other documents in connection therewith, and any and all pre-effective amendments to said registration statement, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing necessary or appropriate to be done in connection therewith, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that said attorney-in-fact and agent, or his substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this registration statement has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Lindsay A. Rosenwald, M.D. Lindsay A. Rosenwald, M.D.	Executive Chairman of the Board	March 27, 2017
/s/ Lucy Lu, M.D. Lucy Lu, M.D.	Interim President, Chief Executive and Director	March 27, 2017
/s/ Scott A. Reines, M.D., Ph.D. Scott A. Reines, M.D., Ph.D.	Interim Chief Medical Officer	March 27, 2017
/s/ David J. Horin David J. Horin	Interim Chief Financial Officer	March 27, 2017
/s/ Michael S. Weiss Michael S. Weiss	Director	March 27, 2017
/s/ Neil Herskowitz Neil Herskowitz	Director	March 27, 2017
/s/ Jeffrey Paley, M.D. Jeffrey Paley, M.D.	Director	March 27, 2017
/s/ Akhtar Samad, M.D., PhD. Akhtar Samad, M.D., PhD.	Director	March 27, 2017
/s/ Jay Kranzler, M.D., PhD Jay Kranzler, M.D., PhD	Director	March 27, 2017

EXHIBIT INDEX

Exhibit No.	Description
1.1	Form of Underwriting Agreement.+
3.1	Second Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc., filed as Exhibit 3.1 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
3.2	Bylaws of Avenue Therapeutics, Inc., filed as Exhibit 3.2 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
4.1	Specimen certificate evidencing shares of Common Stock, filed as Exhibit 4.1 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
4.2	Form of warrant agreement, filed as Exhibit 4.2 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
5.1	Opinion of Alston & Bird LLP.+
10.1	Asset Transfer and License Agreement between Fortress Biotech, Inc. and Revogenex Ireland Limited dated February 17, 2015, filed as Exhibit 10.1 to Form 10-12G/A filed on March 13, 2017 (File No. 000-55556) and incorporated herein by reference.*
10.2	First Amendment to Asset Transfer and License Agreement between Fortress Biotech, Inc. and Revogenex Ireland Limited dated June 23, 2016, filed as Exhibit 10.11 to Form 10-12G/A filed on March 13, 2017 (File No. 000-55556) and incorporated herein by reference.
10.3	Amended and Restated Founders Agreement between Fortress Biotech, Inc. and Avenue Therapeutics, Inc. dated September 13, 2016, filed as Exhibit 10.2 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
10.4	Promissory Note from Avenue Therapeutics, Inc. to NSC Biotech Venture Fund I, LLC, effective as of October 31, 2015, filed as Exhibit 10.3 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
10.5	Promissory Note from Avenue Therapeutics, Inc. to Fortress Biotech, Inc., effective as of March 15, 2015, filed as Exhibit 10.4 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
10.6	Management Services Agreement between Fortress Biotech, Inc. and Avenue Therapeutics, Inc. effective as of February 17, 2015, filed as Exhibit 10.5 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
10.7	Employment Agreement with Dr. Lucy Lu, MD, dated June 10, 2015, filed as Exhibit 10.6 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.#
10.8	Avenue Therapeutics, Inc. 2015 Incentive Plan, filed as Exhibit 10.7 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.
10.9	Consulting Agreement with Dr. Scott A. Reines, dated July 22, 2015, filed as Exhibit 10.8 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.#
10.10	First Amendment to Consulting Agreement with Dr. Scott A. Reines, dated January 25, 2016, filed as Exhibit 10.9 to Form 10-12G filed on January 12, 2017 (File No. 000-55556) and incorporated herein by reference.#
10.11	Second Amendment to Consulting Agreement with Dr. Scott A. Reines, dated August 2, 2016, filed as Exhibit 10.10 to Form 10-12G/A filed on March 13, 2017 (File No. 000-55556) and incorporated herein by reference.#

Exhibit No.	Description
10.12	Third Amendment to Consulting Agreement with Dr. Scott A. Reines, dated February 28, 2017, filed as Exhibit 10.12 to Form 10-12G/A filed on March 13, 2017 (File No. 000-55556) and incorporated herein by reference.#
23.1	Consent of BDO USA, LLP.+
23.2	Consent of Alston & Bird LLP (included in Exhibit 5.1).+
24.1	Power of Attorney (included on signature page).

* Subject to a Confidential Treatment Order.

\# Management Compensation Arrangement.

\+ To be filed by amendment.