

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

FORM S-3 /A  
PRE-EFFECTIVE AMENDMENT NO. 1  
REGISTRATION STATEMENT

UNDER  
THE SECURITIES ACT OF 1933

**AVENUE THERAPEUTICS, INC.**  
(Exact Name of Registrant as Specified in Its Charter)

Delaware  
(State or Other Jurisdiction of  
Incorporation or Organization)

2834  
(Primary Standard Industrial  
Classification Code Number)

47-4113275  
(I.R.S. Employer  
Identification Number)

2 Gansevoort Street, 9<sup>th</sup> 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.  
President & CEO  
2 Gansevoort Street, 9<sup>th</sup> 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:*

Mark F. McElreath, Esq.  
Matthew W. Mamak, Esq.  
Alston & Bird LLP  
90 Park Avenue  
New York, NY 10016  
(212) 210-9400

**Approximate date of commencement of proposed sale to the public:** From time to time after the effective date of this Registration Statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

### CALCULATION OF REGISTRATION FEE

Title Of Each Class Of Securities To Be Registered(1)	Proposed Maximum Aggregate Offering Price(2)	Amount Of Registration Fee(3)
Common Stock, par value \$0.0001 per share(4)	-	-
Preferred Stock, par value \$0.0001 per share(4)	-	-
Warrants	-	-
Debt Securities	-	-
Units(5)	-	-
<b>Total</b>	<b>\$ 75,000,000</b>	<b>\$ 9,337.50</b>

- (1) An indeterminate aggregate initial offering price or number of the securities of each identified class is being registered as may from time to time be offered at indeterminate prices, along with an indeterminate number of securities that may be issued upon exercise, settlement, exchange or conversion of securities offered hereunder, so long as such aggregate initial offering price does not exceed \$75,000,000, less the aggregate dollar amount of all securities previously sold hereunder. Separate consideration may or may not be received for securities that are issuable upon exercise, settlement, conversion or exchange of other securities or that are issued in units with other securities registered hereunder.
- (2) Certain information as to each class of securities to be registered is not specified, in accordance with General Instruction II.D of Form S-3 under the Securities Act. The proposed maximum per unit aggregate offering prices per class of security will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities issued hereunder.
- (3) The registration fee has been calculated in accordance with Rule 457(o) under the Securities Act of 1933, as amended.
- (4) Includes an indeterminate number of shares of common stock or preferred stock as may be issued by the registrant upon exercise, conversion or exchange of any securities that provide for such issuance, or that may from time to time become issuable by reason of any stock split, stock dividend or similar transaction, for which no separate consideration will be received by registrant.
- (5) Each unit will be issued under a unit agreement and will represent an interest in two or more other securities, which may or may not be separable from one another.

**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 Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.**

### EXPLANATORY NOTE

This Amendment No. 1 (the “Amendment”) to the Registration Statement on Form S-3 originally filed by Avenue Therapeutics, Inc. on April 13, 2018 (the “Original Registration Statement”) is being filed solely to amend the information incorporated by reference in the Original Registration Statement. Except as specifically noted above, this Amendment does not modify or update disclosures in the Original Registration Statement.

**The information in this 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 prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.**

**Subject To Completion, Dated May 2, 2018**

**PROSPECTUS**

\$75,000,000



**Common Stock  
Preferred Stock  
Warrants  
Debt Securities  
Units**

---

The following are types of securities that we may offer, issue and sell from time to time, together or separately:

- shares of our common stock;
- shares of our preferred stock;
- warrants;
- debt securities; and
- units consisting of any combination of our common stock, preferred stock, warrants or debt securities.

We may offer these securities in amounts, at prices, and on terms determined at the time of offering, up to an aggregate amount of \$75,000,000. We may sell these securities directly to you through agents we select or through underwriters and dealers we select. If we use agents, underwriters or dealers to sell these securities, we will name them and describe their compensation in a prospectus supplement. See "Plan of Distribution." You should read this prospectus and any prospectus supplement carefully before you invest.

This prospectus provides a general description of the securities we may offer. Each time we sell securities, we will provide specific terms of the securities offered in a supplement to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus and the applicable prospectus supplement carefully, together with additional information described under the heading "Where You Can Find More Information," before you invest in any securities. This prospectus may not be used to consummate a sale of securities unless accompanied by the applicable prospectus supplement.

Our common stock is traded on the Nasdaq Capital Market under the symbol "ATXI." On April 11, 2018, the per share closing price of our common stock as reported on the Nasdaq Capital Market was \$4.85 per share. The aggregate market value of our outstanding common stock held by non-affiliates, computed by reference to the last sold price of \$4.85 per share on the NASDAQ Capital Market on April 11, 2018, is approximately \$31.1 million based on 10,553,045 shares of common stock outstanding, of which 6,409,616 are held by non-affiliates. We have not offered or sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar month period that ends on, and includes, the date of this prospectus.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act and will therefore be subject to reduced reporting requirements.

**Investing in our common stock involves certain risks.** See "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2017, which has been filed with the SEC and is incorporated by reference into this prospectus. You should read the prospectus, any prospectus supplement relating to any specific offering of securities, and all information incorporated by reference herein and therein carefully before you make your investment decision.

**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.**

The date of this prospectus is May , 2018

---

TABLE OF CONTENTS

	<b>PAGES</b>
<a href="#"><u>IMPORTANT INFORMATION ABOUT THIS PROSPECTUS</u></a>	<a href="#"><u>1</u></a>
<a href="#"><u>PROSPECTUS SUMMARY</u></a>	<a href="#"><u>2</u></a>
<a href="#"><u>THE OFFERING</u></a>	<a href="#"><u>3</u></a>
<a href="#"><u>FORWARD-LOOKING STATEMENTS</u></a>	<a href="#"><u>3</u></a>
<a href="#"><u>DESCRIPTION OF SECURITIES WE MAY OFFER</u></a>	<a href="#"><u>4</u></a>
<a href="#"><u>DESCRIPTION OF CAPITAL STOCK</u></a>	<a href="#"><u>5</u></a>
<a href="#"><u>DESCRIPTION OF PREFERRED STOCK</u></a>	<a href="#"><u>6</u></a>
<a href="#"><u>DESCRIPTION OF WARRANTS</u></a>	<a href="#"><u>8</u></a>
<a href="#"><u>DESCRIPTION OF DEBT SECURITIES</u></a>	<a href="#"><u>9</u></a>
<a href="#"><u>DESCRIPTION OF UNITS</u></a>	<a href="#"><u>12</u></a>
<a href="#"><u>PLAN OF DISTRIBUTION</u></a>	<a href="#"><u>13</u></a>
<a href="#"><u>LEGAL MATTERS</u></a>	<a href="#"><u>15</u></a>
<a href="#"><u>EXPERTS</u></a>	<a href="#"><u>16</u></a>
<a href="#"><u>WHERE YOU CAN FIND MORE INFORMATION</u></a>	<a href="#"><u>16</u></a>
<a href="#"><u>INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE</u></a>	<a href="#"><u>16</u></a>

## IMPORTANT INFORMATION 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 is part of a “shelf” registration statement that we filed with the SEC. By using a shelf registration statement, we may sell our securities, as described in this prospectus, from time to time in one or more offerings. We may use the shelf registration statement to offer and sell securities described in this prospectus. Each time we sell securities, we will provide a prospectus or prospectus supplement to this prospectus that contains specific information about the terms of such offering. The prospectus or prospectus supplement may also add, update or change information contained in this prospectus. Before purchasing any securities, you should carefully read both this prospectus and any supplement, together with the additional information incorporated into this prospectus or described under the heading “*Where You Can Find More Information* .”

You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus or prospectus supplement. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, as well as information we previously filed with the SEC and have incorporated by reference, is accurate as of the date on the front cover of this prospectus only, or when such document was filed with the SEC. Our business, financial condition, results of operations and prospects may have changed since the relevant date.

Neither we, nor any of our officers, directors, agents or representatives or underwriters, make any representation to you about the legality of an investment. You should not interpret the contents of this prospectus, any prospectus supplement, 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.

We will not use this prospectus to offer and sell securities unless it is accompanied by a prospectus or prospectus supplement that more fully describes the terms of the offering.

## PROSPECTUS SUMMARY

This summary provides an overview of selected information contained elsewhere or incorporated by reference in this prospectus and does not contain all of the information you should consider before investing in our securities. You should carefully read the prospectus, the information incorporated by reference and the registration statement of which this prospectus is a part in their entirety before investing in our securities, including the information discussed under “Risk Factors” in this prospectus and the documents incorporated by reference and our financial statements and notes thereto that are incorporated by reference in this prospectus. As used in this prospectus, unless the context otherwise indicates, the terms “we,” “our,” “us,” or “the Company” refers to Avenue Therapeutics, Inc., a Delaware corporation.

**The Company** is a specialty pharmaceutical company that acquires, licenses, develops and commercializes products principally for use in the acute/intensive care hospital setting. Our product candidate is intravenous (IV) Tramadol, for the treatment of moderate to moderately severe post-operative pain. In 2016, we completed a pharmacokinetic (PK) study for IV Tramadol in healthy volunteers as well as an end of phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA). In the third quarter of 2017, we initiated a Phase 3 development program of IV Tramadol for the management of post-operative pain. 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 sales revenue from our product candidates.

On June 26, 2017, we completed an initial public offering (IPO) of our common stock, resulting in net proceeds of approximately \$34.2 million after deducting underwriting discounts, and other offering costs.

We have used the proceeds from the IPO to initiate our first Phase 3 trial of IV Tramadol in patients with moderate-to-severe pain following bunionectomy which had its first patient dosed in September 2017. We anticipate that we will have topline data in the second quarter of 2018.

Further, 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.

In December 2017, we initiated 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.

To date, we have not received approval for the sale of our product candidate in the U.S. market and, therefore, have not generated any product sales. In addition, 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 we develop and seek regulatory approval for IV Tramadol in the U.S. As of December 31, 2017, we had an accumulated deficit of approximately \$20.7 million.

**Our principal executive offices are located at 2 Gansevoort Street, 9th Floor, New York, New York 10014, and our telephone number is 781-652-4500. We maintain a website on the Internet at [www.avenuetx.com](http://www.avenuetx.com) and our e-mail address is [info@avenuetx.com](mailto:info@avenuetx.com). Our Internet website, and the information contained on it, are not to be considered part of this prospectus.**

We are a majority controlled subsidiary of Fortress Biotech, Inc. (“Fortress”).

## THE OFFERING

Use of proceeds

We intend to use the net proceeds of any offering as set forth in the applicable prospectus supplement.

Nasdaq Capital Market symbol

ATXI

## FORWARD-LOOKING STATEMENTS

This prospectus includes statements that are, or may be deemed, "forward-looking statements." In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. They appear in a number of places throughout this prospectus and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our history of net operating losses and uncertainty regarding our ability to obtain capital and achieve profitability, our ability to develop and commercialize our product candidates, our ability to advance our development programs, enroll our trials, and achieve clinical endpoints, our ability to use or expand our technology to build a pipeline of product candidates, our ability to obtain and maintain regulatory approval of our product candidates and comply with ongoing regulatory requirements, our ability to successfully operate in a competitive industry and gain market acceptance by physician, provider, patient, and payor communities, our reliance on third parties, unstable economic or market conditions, and our ability to obtain and adequately protect intellectual property rights for our product candidates.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this prospectus. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this prospectus, they may not be predictive of results or developments in future periods.

## **DESCRIPTION OF SECURITIES WE MAY OFFER**

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize all the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If so indicated in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include information in the prospectus supplement, where applicable, about material United States federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed. This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

## DESCRIPTION OF CAPITAL STOCK

The following description summarizes the material terms of our capital stock as of the date of this prospectus. 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 Third Amended and Restated Certificate of Incorporation and our Bylaws, and to the provisions of applicable Delaware law.

Our authorized capital stock consists 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 of which are undesignated Preferred Stock.

As of April 11, 2018, there were 10,553,045, shares of our common stock outstanding held by 11 record stockholders.

### **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.

Our common stock is traded on the Nasdaq Capital Market under the symbol "ATXI." The transfer agent and registrar for our common stock is VStock Transfer, LLC.

## DESCRIPTION OF PREFERRED STOCK

### 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 February 17 of each year, 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.

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).

It is not possible to state the actual effect of the issuance of any shares of preferred stock upon the rights of the holders of common stock until the board of directors determines the specific rights of the holders of preferred stock. However, effects of the issuance of preferred stock include restricting dividends on common stock, diluting the voting power of common stock, impairing the liquidation rights of common stock, and making it more difficult for a third party to acquire us, which could have the effect of discouraging a third party from acquiring, or deterring a third party from paying a premium to acquire, a majority of our outstanding voting stock.

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.

Our common stock has been approved for listing on the NASDAQ Capital Market under the trading symbol “ATXI.”

## DESCRIPTION OF WARRANTS

We may issue warrants to purchase shares of our common stock and/or preferred stock in one or more series together with other securities or separately, as described in each applicable prospectus supplement. As of April 11, 2018 there were 109,288 shares of common stock that may be issued upon exercise of outstanding warrants.

The prospectus supplement relating to any warrants we offer will include specific terms relating to the offering. These terms will include some or all of the following:

- the title of the warrants;
- the aggregate number of warrants offered;
- the designation, number and terms of the shares of common stock purchasable upon exercise of the warrants and procedures by which those numbers may be adjusted;
- the exercise price of the warrants;
- the dates or periods during which the warrants are exercisable;
- the designation and terms of any securities with which the warrants are issued;
- if the warrants are issued as a unit with another security, the date on and after which the warrants and the other security will be separately transferable;
- if the exercise price is not payable in U.S. dollars, the foreign currency, currency unit or composite currency in which the exercise price is denominated;
- any minimum or maximum amount of warrants that may be exercised at any one time;
- any terms relating to the modification of the warrants;
- any terms, procedures and limitations relating to the transferability, exchange or exercise of the warrants; and
- any other specific terms of the warrants.

## DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior, subordinated or junior subordinated and may be convertible. Unless otherwise specified in the applicable prospectus supplement, our debt securities will be issued in one or more series under an indenture to be entered into between us and a trustee. We will issue the debt securities offered by this prospectus and any accompanying prospectus supplement under an indenture to be entered into between us and the trustee identified in the applicable prospectus supplement. The terms of the debt securities will include those stated in the indenture and those made part of the indenture by reference to the Trust Indenture Act of 1939, as in effect on the date of the indenture. We have filed a copy of the form of indenture as an exhibit to the registration statement in which this prospectus is included. The indenture will be subject to and governed by the terms of the Trust Indenture Act of 1939.

The following description briefly sets forth certain general terms and provisions of the debt securities that we may offer. The particular terms of the debt securities offered by any prospectus supplement and the extent, if any, to which these general provisions may apply to the debt securities, will be described in the related prospectus supplement. Accordingly, for a description of the terms of a particular issue of debt securities, reference must be made to both the related prospectus supplement and to the following description.

### Debt Securities

The aggregate principal amount of debt securities that may be issued under the indenture is unlimited. The debt securities may be issued in one or more series as may be authorized from time to time pursuant to a supplemental indenture entered into between us and the trustee or an order delivered by us to the trustee. For each series of debt securities we offer, a prospectus supplement accompanying this prospectus will describe the following terms and conditions of the series of debt securities that we are offering, to the extent applicable:

- title and aggregate principal amount;
- whether the debt securities will be senior, subordinated or junior subordinated;
- applicable subordination provisions, if any;
- provisions regarding whether the debt securities will be convertible or exchangeable into other securities or property of the Company or any other person;
- percentage or percentages of principal amount at which the debt securities will be issued;
- maturity date(s);
- interest rate(s) or the method for determining the interest rate(s);
- whether interest on the debt securities will be payable in cash or additional debt securities of the same series;
- dates on which interest will accrue or the method for determining dates on which interest will accrue and dates on which interest will be payable;
- whether the amount of payment of principal of, premium, if any, or interest on the debt securities may be determined with reference to an index, formula or other method;
- redemption, repurchase or early repayment provisions, including our obligation or right to redeem, purchase or repay debt securities under a sinking fund, amortization or analogous provision;
- if other than the debt securities' principal amount, the portion of the principal amount of the debt securities that will be payable upon declaration of acceleration of the maturity;
- authorized denominations;
- form;

- amount of discount or premium, if any, with which the debt securities will be issued, including whether the debt securities will be issued as “original issue discount” securities;
- the place or places where the principal of, premium, if any, and interest on the debt securities will be payable;
- where the debt securities may be presented for registration of transfer, exchange or conversion;
- the place or places where notices and demands to or upon the Company in respect of the debt securities may be made;
- whether the debt securities will be issued in whole or in part in the form of one or more global securities;
- if the debt securities will be issued in whole or in part in the form of a book-entry security, the depository or its nominee with respect to the debt securities and the circumstances under which the book-entry security may be registered for transfer or exchange or authenticated and delivered in the name of a person other than the depository or its nominee;
- whether a temporary security is to be issued with respect to such series and whether any interest payable prior to the issuance of definitive securities of the series will be credited to the account of the persons entitled thereto;
- the terms upon which beneficial interests in a temporary global security may be exchanged in whole or in part for beneficial interests in a definitive global security or for individual definitive securities;
- the guarantors, if any, of the debt securities, and the extent of the guarantees and any additions or changes to permit or facilitate guarantees of such debt securities;
- any covenants applicable to the particular debt securities being issued;
- any defaults and events of default applicable to the debt securities, including the remedies available in connection therewith;
- currency, currencies or currency units in which the purchase price for, the principal of and any premium and any interest on, such debt securities will be payable;
- time period within which, the manner in which and the terms and conditions upon which the Company or the purchaser of the debt securities can select the payment currency;
- securities exchange(s) on which the debt securities will be listed, if any;
- whether any underwriter(s) will act as market maker(s) for the debt securities;
- extent to which a secondary market for the debt securities is expected to develop;
- provisions relating to defeasance;
- provisions relating to satisfaction and discharge of the indenture;
- any restrictions or conditions on the transferability of the debt securities;
- provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- any addition or change in the provisions related to compensation and reimbursement of the trustee;
- provisions, if any, granting special rights to holders upon the occurrence of specified events;
- whether the debt securities will be secured or unsecured, and, if secured, the terms upon which the debt securities will be secured and any other additions or changes relating to such security; and

- any other terms of the debt securities that are not inconsistent with the provisions of the Trust Indenture Act (but may modify, amend, supplement or delete any of the terms of the indenture with respect to such series of debt securities).

## **General**

One or more series of debt securities may be sold as “original issue discount” securities. These debt securities would be sold at a substantial discount below their stated principal amount, bearing no interest or interest at a rate which at the time of issuance is below market rates. One or more series of debt securities may be variable rate debt securities that may be exchanged for fixed rate debt securities.

United States federal income tax consequences and special considerations, if any, applicable to any such series will be described in the applicable prospectus supplement.

Debt securities may be issued where the amount of principal and/or interest payable is determined by reference to one or more currency exchange rates, commodity prices, equity indices or other factors. Holders of such debt securities may receive a principal amount or a payment of interest that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending upon the value of the applicable currencies, commodities, equity indices or other factors. Information as to the methods for determining the amount of principal or interest, if any, payable on any date, the currencies, commodities, equity indices or other factors to which the amount payable on such date is linked and certain additional United States federal income tax considerations will be set forth in the applicable prospectus supplement.

The term “debt securities” includes debt securities denominated in U.S. dollars or, if specified in the applicable prospectus supplement, in any other freely transferable currency or units based on or relating to foreign currencies.

We expect most debt securities to be issued in fully registered form without coupons and in denominations of \$2,000 and any integral multiples thereof. Subject to the limitations provided in the indenture and in the prospectus supplement, debt securities that are issued in registered form may be transferred or exchanged at the principal corporate trust office of the trustee, without the payment of any service charge, other than any tax or other governmental charge payable in connection therewith.

## **Global Securities**

The debt securities of a series may be issued in whole or in part in the form of one or more global securities that will be deposited with, or on behalf of, a depository identified in the prospectus supplement. Global securities will be issued in registered form and in either temporary or definitive form. Unless and until it is exchanged in whole or in part for the individual debt securities, a global security may not be transferred except as a whole by the depository for such global security to a nominee of such depository or by a nominee of such depository to such depository or another nominee of such depository or by such depository or any such nominee to a successor of such depository or a nominee of such successor. The specific terms of the depository arrangement with respect to any debt securities of a series and the rights of and limitations upon owners of beneficial interests in a global security will be described in the applicable prospectus supplement.

## **Governing Law**

The indenture and the debt securities shall be construed in accordance with and governed by the laws of the State of New York.

## DESCRIPTION OF UNITS

We may issue, in one more series, units comprised of shares of our common stock and/or preferred stock, warrants to purchase common stock and/or preferred stock, debt securities or any combination of those securities. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We may evidence units by unit certificates that we issue under a separate agreement. We may issue the units under a unit agreement between us and one or more unit agents. If we elect to enter into a unit agreement with a unit agent, the unit agent will act solely as our agent in connection with the units and will not assume any obligation or relationship of agency or trust for or with any registered holders of units or beneficial owners of units. We will indicate the name and address and other information regarding the unit agent in the applicable prospectus supplement relating to a particular series of units if we elect to use a unit agent.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described herein; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The other provisions regarding our common stock, preferred stock, warrants and debt securities as described in this section will apply to each unit to the extent such unit consists of shares of our common stock, warrants and/or debt securities.

## PLAN OF DISTRIBUTION

We may sell the securities covered in this prospectus in one or more of the following ways:

- through underwriters or dealers;
- in short or long transactions;
- directly to a limited number of purchasers or to a single purchaser;
- through agents, including via an at-the-market program; or
- through a combination of any of these methods of sale.

Each time that we use this prospectus to sell securities, we will also provide a prospectus supplement that contains the specific terms of the offering. The prospectus supplement will set forth the terms of the offering of the securities, including:

- the name or names of any underwriters, dealers or agents and the amounts of any securities underwritten or purchased by each of them; and
- the purchase price of the securities being offered and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers.

The purchase price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters will be obligated to purchase all of the securities if they purchase any of securities. Only underwriters named in the applicable prospectus supplement shall be underwriters of the securities offered thereby.

We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified applicable date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act of 1933, as amended, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

We may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of securities, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of securities. The third party in such sale transactions will be an underwriter and will be identified in the applicable prospectus supplement (or a post-effective amendment). We may also use underwriters or such other third parties with whom we have a material relationship. We will describe the nature of any such relationship in the applicable prospectus supplement.

## **At-the-Market Offerings**

Upon written instruction from us, after entering into a distribution agency agreement with us, a sales agent may use its commercially reasonable efforts to sell on our behalf, as our agent, the shares of common stock offered as agreed upon by us and the sales agent. We will designate the maximum amount of shares of common stock to be sold through the sales agent, on a daily basis or otherwise as we and the sales agent agree. Subject to the terms and conditions of the applicable distribution agency agreement, the sales agent will use its commercially reasonable efforts to sell, as our sales agent and on our behalf, all of the designated shares of common stock. We may instruct the sales agent not to sell shares of common stock if the sales cannot be effected at or above the price designated by us in any such instruction. We may suspend the offering of shares of common stock under any distribution agency agreement by notifying the sales agent. Likewise, the sales agent may suspend the offering of shares of common stock under the applicable distribution agency agreement by notifying us of such suspension.

We also may sell shares to the sales agent as principal for its own account at a price agreed upon at the time of sale. If we sell shares to the sales agent as principal, we will enter into a separate agreement setting forth the terms of such transaction.

It is contemplated that the distribution agreements entered into with sales agents will allow such sales agents to make sales in privately negotiated transactions and/or under any other method permitted by law, including sales deemed to be an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act, sales made directly on the Nasdaq Capital Market, the existing trading market for our common stock, or sales made to or through a market maker other than on an exchange. The name of any such underwriter or agent involved in the offer and sale of our common stock, the amounts underwritten, and the nature of its obligations to take our common stock will be described in the applicable prospectus supplement.

## **LEGAL MATTERS**

Certain legal matters will be passed upon for us by Alston & Bird LLP, New York, New York. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

## EXPERTS

The financial statements as of December 31, 2017 and 2016 and for the years ended December 31, 2017 and 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 file reports with the SEC on an annual basis using Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K. You may read and copy any such reports and amendments thereto at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for information on the operation of the Public Reference Room. Additionally, the SEC maintains a website that contains annual, quarterly, and current reports, proxy statements, and other information that issuers (including us) file electronically with the SEC. The SEC's website address is <http://www.sec.gov>. You can also obtain copies of materials we file with the SEC from our Internet website found at [www.avenuetx.com](http://www.avenuetx.com). Our stock is quoted on the Nasdaq Capital Market under the symbol "ATXI". We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this prospectus.

## INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with them. This means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this document. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (1) after the date of the initial registration statement, as amended, and prior to effectiveness of the registration statement, and (2) after the date of this prospectus and prior to the termination of this offering. Such information will automatically update and supersede the information contained in this prospectus and the documents listed below; provided, however, that we are not, unless specifically indicated, incorporating any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K, whether listed below or filed in the future, or related exhibits furnished pursuant to Item 9.01 of Form 8-K:

- a) Our Annual Report on Form 10-K for the year ended December 31, 2017;
- b) Our Current Reports on Form 8-K filed with the SEC on each of January 2, 2018, March 1, 2018 and March 28, 2018;
- c) The description of our common stock contained in our registration statement on Form 10-12G filed with the SEC on January 12, 2017;
- d) The description of our common stock contained in our registration statement on Form S-1 filed with the SEC on April 28, 2017; and
- e) The portions of our Definitive Proxy Statement on Schedule 14A filed with the SEC on April 30, 2018 that are incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2017.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

---

\$ 75,000,000



**Avenue Therapeutics, Inc.**

Common Stock  
Preferred Stock  
Warrants  
Debt Securities  
Units

---

PROSPECTUS

---

May , 2018

**PART II**  
**INFORMATION NOT REQUIRED IN PROSPECTUS**

**Item 14. Other Expenses of Issuance and Distribution**

	<b>Amount to Be Paid</b>
U.S. Securities and Exchange Commission registration fee	\$ 9,337.50
FINRA filing fees	\$ *
Legal fees and expenses	*
Accounting fees and expenses	*
Miscellaneous	*
Total	\$ *

\* To be filed by amendment, Form 8-K or Rule 424 filing.

**Item 15. Indemnification of Directors and Officers**

Under the General Corporation Law of the State of Delaware (“DGCL”), a corporation may include provisions in its certificate of incorporation that will relieve its directors of monetary liability for breaches of their fiduciary duty to the corporation, except under certain circumstances, including a breach of the director’s duty of loyalty, acts or omissions of the director not in good faith or which involve intentional misconduct or a knowing violation of law, the approval of an improper payment of a dividend or an improper purchase by the corporation of stock or any transaction from which the director derived an improper personal benefit. The Company’s Third Amended and Restated Certificate of Incorporation eliminates the personal liability of directors to the Company or its stockholders for monetary damages for breach of fiduciary duty as a director with certain limited exceptions set forth in the DGCL.

Section 145 of the DGCL grants to corporations the power to indemnify each officer and director against liabilities and expenses incurred by reason of the fact that he or she is or was an officer or director of the corporation if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The Company’s Third Amended and Restated Certificate of Incorporation and Bylaws provide for indemnification of each officer and director of the Company to the fullest extent permitted by the DGCL. Section 145 of the DGCL also empowers corporations to purchase and maintain insurance on behalf of any person who is or was an officer or director of the corporation against liability asserted against or incurred by him in any such capacity, whether or not the corporation would have the power to indemnify such officer or director against such liability under the provisions of Section 145 of the DGCL.

**Item 16. Exhibits and Financial Statement Schedules**

The exhibits to the Registration Statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

**Item 17. Undertakings**

(a) The undersigned registrant hereby undertakes:

1. To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the “Calculation of Registration Fee” table in the effective registration statement.

2. That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment 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.

3. To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

5. That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(a) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(b) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. *Provided, however,* that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

6. That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(a) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;

(b) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;

(c) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and

(d) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefits plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement 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.

(c) The undersigned registrant hereby undertakes to supplement the prospectus, after the expiration of the subscription period, to set forth the results of the subscription offer, the transactions by the underwriters during the subscription period, the amount of unsubscribed securities to be purchased by the underwriters, and the terms of any subsequent reoffering thereof. If any public offering by the underwriters is to be made on terms differing from those set forth on the cover page of the prospectus, a post-effective amendment will be filed to set forth the terms of such offering.

(e) The undersigned registrant hereby undertakes (1) to use its best efforts to distribute prior to the opening of bids, to prospective bidders, underwriters, and dealers, a reasonable number of copies of a prospectus which at that time meets the requirements of section 10(a) of the Act, and relating to the securities offered at competitive bidding, as contained in the registration statement, together with any supplements thereto, and (2) to file an amendment to the registration statement reflecting the results of bidding, the terms of the reoffering and related matters to the extent required by the applicable form, not later than the first use, authorized by the issuer after the opening of bids, of a prospectus relating to the securities offered at competitive bidding, unless no further public offering of such securities by the issuer and no reoffering of such securities by the purchasers is proposed to be made.

(h) 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 Securities Act of 1933, as amended, 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 Securities Act of 1933, as amended, and will be governed by the final adjudication of such issue.

## SIGNATURES

Pursuant to the requirements of Section 12 of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

### Avenue Therapeutics, Inc.

By: /s/ Lucy Lu, M.D.  
Name: Lucy Lu, M.D.  
Title: President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Lucy Lu, M.D.</u> Lucy Lu, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	May 2, 2018
<u>/s/ Joseph Vazzano*</u> Joseph Vazzano	Vice President of Finance and Corporate Controller (Principal Financial Officer)	May 2, 2018
<u>/s/ Lindsay A. Rosenwald, M.D.*</u> Lindsay A. Rosenwald, M.D.	Executive Chairman of the Board	May 2, 2018
<u>/s/ Michael S. Weiss*</u> Michael S. Weiss	Director	May 2, 2018
<u>/s/ Neil Herskowitz*</u> Neil Herskowitz	Director	May 2, 2018
<u>/s/ Jeffrey Paley, M.D.*</u> Jeffrey Paley, M.D.	Director	May 2, 2018
<u>/s/ Akhtar Samad, M.D., Ph.D.*</u> Akhtar Samad, M.D., Ph.D.	Director	May 2, 2018
<u>/s/ Jay Kranzler, M.D., Ph.D.*</u> Jay Kranzler, M.D., Ph.D.	Director	May 2, 2018

\* By Lucy Lu, M.D., as attorney in fact

## EXHIBIT INDEX

Exhibit No.	Description
1.1	Underwriting Agreement. ♦
<a href="#">3.1</a>	<a href="#">Third Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc., filed as Exhibit 3.1 to Form 8-K filed on June 27, 2017 (File No. 001-38114) and incorporated herein by reference.</a>
<a href="#">3.2</a>	<a href="#">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.</a>
<a href="#">4.1</a>	<a href="#">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.</a>
4.2	Form of Preferred Stock Designation. ♦
4.3	Form of Warrant Agreement. ♦
4.4	Form of Common Stock Warrant Agreement and Warrant Certificate. ♦
<a href="#">4.5†</a>	<a href="#">Form of Indenture.</a>
4.6	Form of Note. ♦
4.7	Form of Unit Agreement. ♦
<a href="#">5.1†</a>	<a href="#">Opinion of Alston &amp; Bird LLP.</a>
<a href="#">23.1†</a>	<a href="#">Consent of BDO USA, LLP, Independent Registered Accounting Firm.</a>
<a href="#">23.2†</a>	<a href="#">Consent of Alston &amp; Bird LLP (to be included in Exhibit 5.1).</a>
<a href="#">24.1†</a>	<a href="#">Power of Attorney.</a>
25.1	Statement of Eligibility of Trustee Under Debt Indenture.*

---

\* To be filed, if necessary separately pursuant to Section 305(b)(2) of the Trust Indenture Act of 1939.

♦ To be filed by amendment or as an exhibit to a document to be incorporated by reference herein in connection with an offering of our securities to the extent applicable.

† Incorporated by reference from our Registration Statement on Form S-3 filed on April 13, 2018.