



Up to \$3,850,000

Common Stock

We have entered into a sales agreement (the “sales agreement”) dated May 10, 2024, with H.C. Wainwright & Co., LLC, as Agent (“Wainwright”), relating to the sale of shares of our common stock, par value \$0.0001 per share (“common stock”) having an aggregate purchase price of \$3,850,000. In accordance with the terms of the sales agreement, pursuant to this prospectus supplement and upon our delivery of a placement notice to the Agent, we may offer and sell shares of our common stock having an aggregate offering price of up to \$3,850,000 from time to time through the Agent.

Our common stock is listed on the Nasdaq Capital Market under the symbol “ATXI.” On May 8, 2024, the closing sale price of our common stock on the Nasdaq Capital Market was \$4.40 per share.

Sales of our common stock, if any, under this prospectus supplement will be made by any method permitted that is deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended (the “Securities Act”). The Agent is not required to sell any specific number or dollar amount of securities, but will act as our sales agent using commercially reasonable efforts consistent with their normal trading and sales practices to sell on our behalf all of the shares of common stock requested to be sold by us, on mutually agreed terms between the Agent and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The Agent will be entitled to compensation under the terms of the sales agreement at a commission rate of up to 3% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of our common stock on our behalf, each Agent will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of the Agent may be deemed to be underwriting commissions or discounts. See “Plan of Distribution” beginning on page [S-17](#) for additional information regarding the compensation to be paid to the Agent. We have also agreed to provide indemnification and contribution to the Agent with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended (the “Exchange Act”).

As of May 10, 2024, the aggregate market value of our outstanding common stock held by non-affiliates, or public float calculated for purposes of General Instruction I.B.6 of Form S-3, was approximately \$11,600,000, based on 940,809 shares of outstanding common stock as of May 8, 2024, of which approximately 52,477 shares were held by affiliates, and a price of \$13.125 per share, which was the price at which our common stock was last sold on the Nasdaq Capital Market on March 12, 2024. We have not sold any securities pursuant to General Instruction I.B.6 of Form S-3 during the prior 12-calendar month period that ends on and includes the date of this prospectus supplement (excluding this offering). Accordingly, based on the foregoing, we are currently eligible under General Instruction I.B.6 of Form S-3 to offer and sell shares of our common stock having an aggregate offering price of up to approximately \$3,850,000. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million.

Investing in our common stock involves a high degree of risk. See “Risk Factors” beginning on page [S-10](#) of this prospectus supplement and page [3](#) of the accompanying prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement concerning factors you should consider before investing in our common stock.

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

H.C. Wainwright & Co.

The date of this prospectus supplement is May 10, 2024.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process. Under this prospectus supplement, we may offer shares of our common stock having an aggregate offering price set forth on the cover page hereof, from time to time at prices and on terms to be determined by market conditions at the time of offering.

Before buying any of the shares of common stock offered hereby, we urge you to read carefully this prospectus supplement, the accompanying base prospectus and all of the information incorporated herein by reference in this prospectus supplement and the accompanying base prospectus, as well as the additional information described below under the heading “*Incorporation of Certain Information by Reference.*” These documents contain important information that you should consider when making your investment decision.

We provide information to you about this offering of our common stock in two separate documents that are bound together: (1) this prospectus supplement, which describes the specific details regarding this offering; and (2) the accompanying base prospectus, which provides general information, some of which may not apply to this offering. Generally, when we refer to this “prospectus,” we are referring to both documents combined. If information in this prospectus supplement is inconsistent with the accompanying base prospectus, you should rely on this prospectus supplement. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference in this prospectus supplement that was filed with the SEC before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement, provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in this prospectus supplement—the statement in the document having the later date modifies or supersedes the earlier statement.

We have not, and the sales agent has not, authorized anyone to provide you with information other than the information that we have provided or incorporated by reference in this prospectus supplement, the accompanying base prospectus or any other prospectus supplement and your reliance on any unauthorized information or representation is at your own risk. This prospectus supplement may be used only in jurisdictions where offers and sales of these securities are permitted. You should assume that the information appearing in this prospectus supplement is accurate only as of the date of this prospectus supplement and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement, or any sale of our common stock. Our business, financial condition and results of operations may have changed since those dates.

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

Unless otherwise indicated, information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus concerning our industry, including our general expectations and market opportunity, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry’s future performance are necessarily uncertain due to a variety of factors, including those described in section of this prospectus supplement titled “*Risk Factors.*” These and other factors could cause our future performance to differ materially from our assumptions and estimates.

We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the securities offered hereby and only under circumstances and in jurisdictions where it is lawful to do so. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus supplement, accompanying prospectus, and any free writing prospectuses prepared by or on behalf of us or to which we have referred you or are incorporated by reference. This prospectus supplement is not an offer to sell securities, and it is not soliciting an offer to buy securities, in any jurisdiction where the offer or sale is not permitted.

This prospectus supplement contains references to trademarks, trade names and service marks belonging to other entities. Solely for convenience, trademarks, trade names and service marks referred to in this prospectus may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that the applicable licensor will not assert, to the fullest extent under applicable law, its rights to these trademarks and trade names. We do not intend our use or display of other entities’ trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entities.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement contains predictive or “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of current or historical fact contained in this prospectus, including statements that express our intentions, plans, objectives, beliefs, expectations, strategies, predictions or any other statements relating to our future activities or other future events or conditions are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “will,” “should,” “would” and similar expressions, as they relate to us, are intended to identify forward-looking statements.

These statements are based on current expectations, estimates and projections made by management about our business, our industry and other conditions affecting our financial condition, results of operations or business prospects. These statements are not guarantees of future performance and involve risks, uncertainties and assumptions that are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed or forecasted in, or implied by, the forward-looking statements due to numerous risks and uncertainties. Factors that could cause such outcomes and results to differ include, but are not limited to, risks and uncertainties arising from:

- the fact that we currently have no drug products for sale and that our success is dependent on our product candidates receiving regulatory approval and being successfully commercialized;
- the possibility that serious adverse or unacceptable side effects are identified during the development of our current or future product candidates, such that we would need to abandon or limit development of some of our product candidates;
- our ability to successfully develop, partner, or commercialize any of our current or future product candidates including AJ201, IV tramadol, and BAER-101;
- the substantial doubt raised about our ability to continue as a going concern, which may hinder our ability to obtain future financing;
- the significant losses we have incurred since inception and our expectation that we will continue to incur losses for the foreseeable future;
- our need for substantial additional funding, which may not be available to us on acceptable terms, or at all, which unavailability could force us to delay, reduce, or eliminate our product development programs or commercialization efforts;
- our reliance on third parties for several aspects of our operations;
- our reliance on clinical data and results obtained by third parties that could ultimately prove to be inaccurate, unreliable, or unacceptable to regulatory authorities;
- the possibility that we may not receive regulatory approval for any or all of our product candidates, or that such approval may be significantly delayed due to scientific or regulatory reasons;
- the fact that even if one or more of our product candidates receives regulatory approval, they will remain subject to substantial regulatory scrutiny;
- the effects of current and future laws and regulations relating to fraud and abuse, false claims, transparency, health information privacy and security, and other healthcare laws and regulations;
- the effects of competition for our product candidates and the potential for new products to emerge that provide different or better therapeutic alternatives for our targeted indications;
- the possibility that the government or third-party payors fail to provide adequate coverage and payment rates for our product candidates or any future products;
- our ability to establish sales and marketing capabilities or to enter into agreements with third parties to market and sell our product candidates;
- our exposure to potential product liability claims;
- related to the protection of our intellectual property and our potential inability to maintain sufficient patent protection for our technology and products;
- our ability to maintain compliance with the obligations under our intellectual property licenses and funding arrangements with third parties, without which licenses and arrangements we could lose rights that are important to our business;
- the fact that Fortress Biotech, Inc. (“Fortress”) controls a majority of the voting power of our outstanding capital stock and has rights to receive significant share grants annually; and
- the risks described under the section titled “Risk Factors” in this Annual Report and in other filings we make with the SEC.

The forward-looking statements contained in this report reflect our views and assumptions as of the effective date of this report. New risks and uncertainties arise from time to time, and it is impossible for us to predict these events or how they may affect us. Except as required by law, we assume no responsibility for updating any forward-looking statements to reflect events or circumstances that may arise after the date of this report, except as required by applicable law.

We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

MARKET AND INDUSTRY DATA AND FORECASTS

We obtained the industry and market data used throughout this prospectus supplement and in the other documents incorporated by reference into this prospectus supplement from our own internal estimates and research, as well as from independent market research, industry and general publications and surveys, governmental agencies, publicly available information and research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of our industry and market, which we believe to be reasonable. In some cases, we do not expressly refer to the sources from which this data is derived. In addition, while we believe the industry and market data included in this prospectus supplement is reliable and based on reasonable assumptions, such data involve material risks and other uncertainties and are subject to change based on various factors, including those discussed in this prospectus supplement in the section titled "*Risk Factors*," as well as those described in the documents incorporated by reference into this prospectus supplement and the accompany prospectus. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties or by us.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere in or incorporated by reference into this prospectus supplement. Because this is a summary, it may not contain all of the information that may be important to you and to your investment decision. The following summary is qualified in its entirety by the more detailed information and financial statements and notes thereto included elsewhere in this prospectus supplement and the documents incorporated herein by reference and other documents to which we refer. You should read “Risk Factors” beginning on page [S-10](#) of this prospectus supplement, as well as the information appearing under the caption “Item 1A. Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as may be updated by our subsequently filed Exchange Act reports, for more information about important risks that you should consider carefully before buying our securities.

References in this prospectus to the “Company,” “we,” “us,” “our” and similar words refer to Avenue Therapeutics, Inc.

Our Business

Overview and Product Candidate Development

We are a specialty pharmaceutical company focused on the development and commercialization of therapies for the treatment of neurologic diseases. Our product candidates include AJ201 for the treatment of spinal and bulbar muscular atrophy (“SBMA”, also known as Kennedy’s Disease), intravenous tramadol (“IV tramadol”) for the treatment of post-operative acute pain, and BAER-101 for the treatment of epilepsy and panic disorders.

AJ201

In February 2023, we announced that we entered into a license agreement (the “AnnJi License Agreement”) with AnnJi Pharmaceutical Co., Ltd. (“AnnJi”) whereby the Company obtained an exclusive license from AnnJi to intellectual property rights pertaining to the molecule known as JM17, which activates Nrf1 and Nrf2, enhances androgen receptor degradation and underlies AJ201, a clinical product candidate currently in a Phase 1b/2a clinical trial in the United States (“U.S.”) for the treatment of SBMA, also known as Kennedy’s Disease.

AJ201 is a novel, first-in-class asset in development for the treatment of SBMA. It was designed to modify SBMA through multiple mechanisms, including degradation of the mutant androgen receptor (“AR”) protein and stimulation of the Nrf1 and Nrf2 pathways, which are involved in protecting cells from oxidative stress that can lead to cell death. AJ201 is currently being studied in a Phase 1b/2a multicenter, randomized, double-blind clinical trial in six clinical sites across the U.S., which aims to evaluate the safety, pharmacokinetic (“PK”) and pharmacodynamic (“PD”) data and clinical response of AJ201 in patients suffering from SBMA.

Under the AnnJi License Agreement, in exchange for exclusive rights to the intellectual property underlying the AJ201 product candidate, the Company paid an initial cash license fee of \$3.0 million, of which \$2.0 million was paid on April 27, 2023 and \$1.0 million was paid on September 8, 2023. The Company also became obligated to issue shares of its common stock and make additional payments over the course of the AnnJi License Agreement including reimbursement payments of up to \$10.8 million in connection with the product’s Phase 1b/2a clinical trial.

In connection with the signing of the AnnJi License Agreement, the Company agreed to issue 831,618 shares of its common stock to AnnJi (the “First Tranche Shares”), and then to issue an additional 276,652 shares of common stock upon enrollment of the eighth patient in the ongoing Phase 1b/2a SBMA clinical trial (the “Second Tranche Shares” and, together with the First Tranche Shares, the “Consideration Shares”). As of the date of this prospectus, all of the Consideration Shares have been issued. The license provided under the AnnJi License Agreement is exclusive as to all oral forms of AJ201 for use in all indications (other than androgenetic alopecia and Alzheimer’s disease) in the United States, Canada, the European Union, the United Kingdom and Israel. The AnnJi License Agreement also contains customary representations and warranties and provisions related to confidentiality, diligence, indemnification and intellectual property protection. The Company will initially be obligated to obtain both clinical and commercial supply of AJ201 exclusively through AnnJi. In connection with the execution of the AnnJi License Agreement, we entered into a registration rights agreement pursuant to which the Company agreed to file a registration statement to register the resale of the Consideration Shares. The Company filed such registration statement on Form S-3 on June 16, 2023, and the registration statement was subsequently declared effective by the SEC on June 27, 2023.

In July 2023, we announced the first patient was dosed in the Phase 1b/2a trial of AJ201. The 12-week, multicenter, randomized, double-blind Phase 1b/2a clinical trial of AJ201 enrolled 25 patients, randomly assigned to AJ201 (600 mg/day) or placebo. The primary endpoint of the study is to assess the safety and tolerability of AJ201 in subjects with clinically and genetically defined SBMA. Secondary endpoints include pharmacodynamic data measuring change from baseline in mutant AR protein levels in skeletal muscle and changes in the fat and muscle composition as seen on MRI scans, which are believed to be biomarkers indicating likelihood for longer term clinical improvement. Further details about this study can be found at ClinicalTrials.gov (Identifier: NCT05517603). Information on clinicaltrials.gov does not constitute part of this prospectus.

In September 2023, we announced the eighth patient was enrolled and pursuant to the License Agreement, we issued the Second Tranche Shares to AnnJi. In January 2024, we announced the completion of enrollment for the Phase 1b/2a trial with topline data anticipated in the second quarter of 2024.

IV Tramadol

In February 2022, we had our Advisory Committee meeting with the U.S. Food and Drug Administration (“FDA”) regarding IV tramadol. In the final part of the public meeting, the Advisory Committee voted yes or no on the following question: “Has the Applicant submitted adequate information to support the position that the benefits of their product outweigh the risks for the management of acute pain severe enough to require an opioid analgesic in an inpatient setting?” The results were 8 yes votes and 14 no votes. In March 2022, we received an Appeal Denied Letter from the Office of New Drugs (“OND”) of the FDA in response to a formal dispute resolution request (“FDRR”). In August 2022, the Company participated in a Type A Meeting with the FDA Division of Anesthesia, Analgesia, and Addiction Products (“DAAAP”) regarding a briefing document submitted that presented a study design the Company believed would have the potential to address the comments and deficiencies noted in the Letter. The meeting on August 9, 2022 was a collaborative discussion on the study design and potential path forward. We incorporated the FDA’s suggestions from the meeting minutes and submitted a detailed study protocol.

The Company participated in a Type C meeting with the FDA in March 2023 to discuss a proposed study protocol to assess the risk of respiratory depression related to opioid stacking on IV tramadol relative to an approved opioid analgesic. We announced in April 2023 that the Company received official meeting minutes from the Type C meeting with the FDA. The Type C meeting minutes indicate that the FDA and the Company are in agreement with a majority of the proposed protocol items and are in active discussion about remaining open items. The minutes indicate that the FDA also agrees that a successful study will support the submission of a complete response to the second Complete Response Letter for IV tramadol pending final agreement on a statistical analysis plan and a full review of the submitted data in the complete response as well as concurrence from the DAAAP.

In January 2024, we announced that we reached final agreement with the FDA on the Phase 3 safety study protocol and statistical analysis approach, including the primary endpoint. The final non-inferiority study is designed to assess the theoretical risk of opioid-induced respiratory depression related to opioid stacking on IV tramadol compared to IV morphine. The study will randomize approximately 300 post bunionectomy patients to IV tramadol or IV morphine for pain relief administered during a 48-hour post-operative period. Of note, IV tramadol demonstrated safety and efficacy in this same surgical model in two Phase 3 efficacy trials. Patients will have access to IV hydromorphone, a Schedule II opioid, for rescue of breakthrough pain. The primary endpoint is a composite of elements indicative of respiratory depression.

We plan to initiate the study as soon as possible, subject to having the necessary financing.

Recent Developments

Reverse Stock Split

On April 25, 2024, the Company filed a Certificate of Amendment to its Third Amended and Restated Certificate of Incorporation (the “Amendment”) with the Secretary of State of the State of Delaware to effect a 1-for-75 reverse stock split (the “Reverse Stock Split”) of the Company’s shares of common stock, \$0.0001 par value (the “common stock”). As previously disclosed in a Definitive Information Statement on Schedule 14C filed with the SEC on March 18, 2024 (the “Information Statement”), the Company’s stockholders approved the Reverse Stock Split within a range of between 30-for-1 and 75-for-1, such ratio to be determined by the Board of Directors of the Company (the “Board”), which the Board also approved. On April 10, 2024, the Board selected the 1-for-75 reverse stock split ratio. As a result of the Reverse Stock Split, every 75 shares of the Company’s pre-reverse split common stock was combined and reclassified as one share of common stock. Proportionate voting rights and other rights of common stockholders were not affected by the reverse. No fractional shares were issued in connection with the Reverse Stock Split. Instead, stockholders who would otherwise be entitled to receive fractional shares because they hold a number of shares of common stock that is not evenly divided by the reverse split ratio automatically had their fractional shares rounded up to the next whole share in lieu of such fractional shares. Cash was not paid for fractional shares. The Reverse Stock Split became effective on April 26, 2024, and the common stock was quoted on the Nasdaq Capital Market on a post-split basis at the open of business on April 26, 2024. The Company’s post-reverse split common stock has a new CUSIP number, 05360L403, but the par value and other terms of the common stock were not affected by the Reverse Stock Split. All share figures in this prospectus give effect to the 1-for-75 Reverse Stock Split.

Warrant Inducement

On April 28, 2024, the Company entered into inducement offer letter agreements (the “Inducement Letters”) with (i) certain investors (the “October 2022 Investors”) that held certain outstanding warrants to purchase up to an aggregate of 27,271 shares of common stock, originally issued to the October 2022 Investors on October 11, 2022 (the “October 2022 Warrants”); (ii) certain investors (the “November 2023 Investors”) that held certain outstanding Series A and Series B warrants to purchase up to an aggregate of 221,333 shares of common stock, originally issued to the November 2023 Investors on October 31, 2023 (the “November 2023 Warrants”); and (iii) certain investors (the “**January 2024 Investors**”) and, collectively with the October 2022 Investors and November 2023 Investors, the “**Holder**s”) that held certain outstanding Series A and Series B warrants to purchase up to an aggregate of 441,076 shares of common stock, originally issued to January 2024 Investors on January 9, 2024 (the “January 2024 Warrants,” and, collectively with the October 2022 Warrants and November 2023 Warrants, the “Existing Warrants”). The October 2022 Warrants had an exercise price of \$116.25 per share, the November 2023 Warrants had an exercise price of \$22.545 per share, and the January 2024 Warrants had an exercise price of \$22.545 per share.

Pursuant to the Inducement Letters, the Holders agreed to exercise for cash the Existing Warrants at a reduced exercise price of \$6.20 per share in partial consideration for the Company’s agreement to issue in a private placement (x) new Series C common stock purchase warrants (the “New Series C Warrants”) to purchase up to 689,680 shares of common stock (the “New Series C Warrant Shares”) and (y) new Series D common stock Purchase Warrants (the “New Series D Warrants”) and, together with the New Series C Warrants, the “New Warrants”) to purchase up to 689,680 shares of common stock (the “New Series D Warrant Shares” and, together with the New Series C Warrant Shares, the “New Warrant Shares”). The Holders also agreed to make a payment of \$0.125 per New Warrant Share (the “Additional Warrant Consideration”).

The closing of the transactions contemplated pursuant to the Inducement Letters occurred on May 1, 2024 (the “Closing Date”). The Company received aggregate gross proceeds of approximately \$4.4 million from the exercise of the Existing Warrants by the Holders and the payment of the Additional Warrant Consideration, before deducting placement agent fees and other expenses payable by the Company. The Company intends to use the net proceeds for general corporate purposes.

The Company engaged H.C. Wainwright & Co., LLC (“H.C. Wainwright”) to act as its exclusive agent in connection with the transactions summarized above and paid H.C. Wainwright a cash fee equal to 7.0% of the aggregate gross proceeds from the exercise of the Existing Warrants at the reduced exercise price and the Additional Warrant Consideration. In addition, the Company (i) reimbursed H.C. Wainwright for \$50,000 of the fees and expenses of H.C. Wainwright’s legal counsel and other of its out-of-pocket expenses, (ii) reimbursed H.C. Wainwright for its non-accountable expenses in the amount of \$35,000, and (iii) paid a management fee equal to 1.0% of the gross proceeds raised. The Company also issued to H.C. Wainwright or its designees (“PA Warrant Holders”) placement agent warrants (the “Placement Agent Warrants”) to purchase up to 41,381 shares of common stock (the “Placement Agent Warrant Shares”). The Placement Agent Warrants have the same terms as the New Series C Warrants, except that the Placement Agent Warrants have an exercise price equal to \$7.75 per share.

The original sale or resale of the shares of common stock underlying the Existing Warrants have been registered pursuant to an existing registration statements on Form S-1, as amended (File Nos. 333-267206 and 333-275462), and Form S-3 (File No. 333-276671), declared effective by the SEC on October 6, 2022, October 31, 2023 and February 1, 2024, respectively.

The Company filed a registration statement on Form S-3 with the SEC providing for the resale of the New Warrant Shares (the “Resale Registration Statement”) on May 6, 2024, which was declared effective on May 10, 2024.

Pursuant to the Inducement Letters, for a period of twelve (12) months following the Closing Date, the Company agreed not to issue or enter into an agreement to effect a Variable Rate Transaction (as defined in the Inducement Letters), subject to certain exceptions.

Corporate Information

We are a majority-controlled subsidiary of Fortress. Baergic Bio is our sole subsidiary.

Avenue Therapeutics, Inc. was incorporated in Delaware on February 9, 2015. Our executive offices are located at 1111 Kane Concourse, Suite 301, Bay Harbor Islands Florida, 33154. Our telephone number is (781) 652-4500, and our email address is info@avenuetx.com. Information on our website, or any other website, is not incorporated by reference in this prospectus. We have included our website address in this prospectus solely as an inactive textual reference. We are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. You may obtain any of the documents filed by us with the SEC at no cost from the SEC’s website at www.sec.gov.

THE OFFERING

Securities offered by us	Shares of our common stock having an aggregate offering price of up to \$3,850,000.
Common stock to be outstanding after this offering⁽¹⁾	Up to 1,815,809 shares, assuming sales of shares of our common stock in this offering at an offering price of \$4.40 per share, which was the last reported sale price of our common stock on the Nasdaq Capital Market on May 8, 2024. The actual number of shares of common stock issued will vary depending on the sales price under this offering.
Plan of Distribution	“At the market offering” that may be made from time to time on the Nasdaq Capital Market or such other national securities exchange on which our common stock is then listed, through the Agent, acting as our sales agent. See the section titled “ <i>Plan of Distribution</i> ” on page S-17 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, for general corporate purposes and working capital requirements, which may include, among other things, the advancement of our product candidates to obtain regulatory approval from the FDA. However, we will have broad discretion to allocate the net proceeds of this offering. See “ <i>Use of Proceeds</i> ” on page S-14 of this prospectus supplement.
Risk Factors	Any investment in the common stock offered hereby is speculative and involves a high degree of risk. You should carefully consider the information set forth under “ <i>Risk Factors</i> ” in this prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus supplement.
Nasdaq Capital Market symbol	“ATXI”
(1) The number of shares of common stock to be outstanding after this offering is based on 940,809 shares of our common stock outstanding as of May 8, 2024, and excludes:	
	<ul style="list-style-type: none">• 1,476,200 shares of common stock issuable upon exercise of outstanding warrants having a weighted-average exercise price of \$8.64 per share;• 1,028 shares of common stock issuable upon the vesting and settlement of outstanding restricted stock award/units;• 44,701 shares of common stock reserved for issuance and available for future grant under our 2015 Incentive Plan;• 22,474 shares of common stock issuable upon the exercise of stock options with a weighted-average exercise price of \$85.50 per share;• 223 shares of common stock issuable upon conversion of the Class A Preferred Stock, at the holders’ election;• 430,912 shares of common stock held in abeyance;• 17,937 shares of common stock issuable to Fortress pursuant to the Amended and Restated Founders Agreement between Fortress and the Company (the “Founders Agreement”) for warrant exercises; and• 21,875 shares of common stock issuable to Fortress pursuant to the Founders Agreement following the closing of this offering.
Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding stock options or warrants and no settlement of the restricted stock units described above.	

RISK FACTORS

Our business, results of operations and financial condition and the industry in which we operate are subject to various risks. Accordingly, investing in our securities involves a high degree of risk. This prospectus supplement does not describe all of those risks. You should consider the risk factors described in this prospectus supplement below, as well as those described under the caption “Risk Factors” in the documents incorporated by reference herein, including our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, together with the other information contained or incorporated by reference in this prospectus supplement.

We have described below and in the documents incorporated by reference herein the most significant risk factors applicable to us, but they do not constitute all of the risks that may be applicable to us. New risks may emerge from time to time, and it is not possible for us to predict all potential risks or to assess the likely impact of all risks. Before making an investment decision, you should carefully consider these risks as well as other information we include or incorporate by reference in this prospectus supplement. This prospectus supplement also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below. See the section titled “Cautionary Note Regarding Forward-Looking Statements.”

Additional Risks Related to Our Common Stock And This Offering

The actual number of shares we will issue and gross proceeds resulting from those sales, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver a placement notice to the Agent at any time throughout the term of the sales agreement. The number of shares that are sold by the Agent after delivering a placement notice will fluctuate based on the market price of our common stock during the sales period and limits we set with the Agent in any instruction to sell shares, and the demand for our common stock during the sales period. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares or the gross proceeds to be raised in connection with those sales, if any, that will be ultimately issued.

The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

We are selling the securities offered in this prospectus supplement on a “best efforts” basis and may not be able to sell any of the securities offered herein.

We have engaged the Agent to act as our sales agent in connection with this offering. While the Agent will use its reasonable best efforts to arrange for the sale of the securities, the Agent is under no obligation to purchase any of the securities. As a result, there are no firm commitments to purchase any of the securities in this offering. Consequently, there is no guarantee that we will be capable of selling all, or any, of the securities being offered hereby.

We will have broad discretion in the use of proceeds of this offering designated for general corporate purposes and working capital requirements.

Our management will have broad discretion over the use and investment of the net proceeds of this offering. Accordingly, investors in this offering have only limited information concerning our management’s specific intentions and will need to rely upon the judgment of our management with respect to the use of proceeds. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business and cause the price of our securities to decline. Pending the application of these funds, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

If the price of our common stock fluctuates significantly, your investment could lose value.

Although our common stock is listed on Nasdaq Capital Market, we cannot assure you that an active public market will continue for our common stock. If an active public market for our common stock does not continue, the trading price and liquidity of our common stock will be materially and adversely affected. If there is a thin trading market or “float” for our stock, the market price for our common stock may fluctuate significantly more than the stock market as a whole. Without a large float, our common stock would be less liquid than the stock of companies with broader public ownership and, as a result, the trading prices of our common stock may be more volatile. In addition, in the absence of an active public trading market, investors may be unable to liquidate their investment in us. Furthermore, the stock market is subject to significant price and volume fluctuations, and the price of our common stock could fluctuate widely in response to several factors, including:

- our quarterly or annual operating results;
- changes in our earnings estimates;
- investment recommendations by securities analysts following our business or our industry;
- additions or departures of key personnel;
- our failure to achieve operating results consistent with securities analysts’ projections; and
- changes in industry, general market or economic conditions.

The stock market has experienced extreme price and volume fluctuations in recent years that have significantly affected the quoted prices of the securities of many companies, including companies in our industry. The changes often appear to occur without regard to specific operating performance. The price of our common stock could fluctuate based upon factors that have little or nothing to do with our company and these fluctuations could materially reduce our stock price.

We do not intend to pay dividends on our common stock, so any returns will be limited to increases, if any, in our stocks value. Your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any future determination to declare dividends will be made at the discretion of our Board and will depend on, among other factors, our financial condition, operating results, capital requirements, general business conditions and other factors that our Board may deem relevant. Any return to stockholders will therefore be limited to the appreciation in the value of their stock, if any.

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

Investors purchasing shares of our common stock in this offering will pay a price per share that substantially exceeds the pro forma as adjusted net tangible book value per share. As a result, investors purchasing shares of our common stock in this offering will incur immediate dilution of \$1.00 per share, representing the difference between the assumed offering price of \$4.40, the last reported sales price of our common stock on the Nasdaq Capital Market on May 8, 2024, and our pro forma as adjusted net tangible book value per share as of December 31, 2023. To the extent outstanding options or warrants to purchase our common stock are exercised and to the extent that we issue to Fortress the shares of common stock issuable pursuant to the Founders Agreement following the closing of this offering, new investors may incur further dilution. For more information on the dilution you may experience as a result of investing in this offering, see the section of this prospectus supplement entitled “*Dilution.*”

If we sell common stock or preferred stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time-to-time issue additional shares of common stock or preferred stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, common stock or preferred stock. If we issue common stock or securities convertible into common stock, the holders of our common stock would experience additional dilution and, as a result, our stock price may decline.

There is substantial doubt about our ability to continue as a going concern, which may hinder our ability to obtain future financing.

We are not yet generating revenue, have incurred substantial operating losses since our inception and expect to continue to incur significant operating losses for the foreseeable future as we execute on our product development plan and may never become profitable. As of December 31, 2023, we had cash and cash equivalents of \$1.8 million and an accumulated deficit of \$90.9 million, and, as of December 31, 2022, we had cash and cash equivalents of \$6.7 million and an accumulated deficit of \$80.5 million. We do not believe that our cash is sufficient for the next twelve months. As a result, there is substantial doubt about our ability to continue as a going concern. Our ability to continue as a going concern will depend on our ability to obtain additional funding, as to which no assurances can be given. This offering is being conducted on a best-efforts basis, from time to time as market conditions warrant, and we may sell fewer than all of the securities offered hereby and may receive significantly less in net proceeds from this offering than the maximum amount set forth on the cover page of this prospectus supplement. Furthermore, even if we sell all the securities offered hereby and raise the maximum amount of proceeds, we may need to raise additional capital to fund our operations and continue to support our planned development and commercialization activities. If we are unable to obtain funds when needed or on acceptable terms, we may be required to curtail our current development programs, cut operating costs, forgo future development and other opportunities or even terminate our operations.

If we fail to satisfy applicable listing standards of The Nasdaq Capital Market, our common stock could be delisted from The Nasdaq Capital Market.

On May 19, 2023, we received a deficiency letter (the “Nasdaq Stockholders’ Equity Letter”) from the Listing Qualifications Department (the “Staff”) of The Nasdaq Stock Market LLC (“Nasdaq”), notifying us that we are not in compliance with Nasdaq Listing Rule 5550(b)(1), which requires us to maintain a minimum of \$2,500,000 in stockholders’ equity for continued listing on The Nasdaq Capital Market (the “Stockholders’ Equity Requirement”), nor in compliance with either of the alternative listing standards, market value of listed securities of at least \$35 million or net income of \$500,000 from continuing operations in the most recently completed fiscal year, or in two of the three most recently completed fiscal years. Pursuant to the Nasdaq Stockholders’ Equity Letter, we had 45 calendar days from the date of the Nasdaq Stockholders’ Equity Letter to submit a plan to regain compliance. On July 3, 2023, we submitted a compliance plan (the “Compliance Plan”). On July 17, 2023, the Staff granted the Company’s request for an extension of the deadline to regain compliance with the Rule to November 15, 2023. The Company was unable to demonstrate compliance with the Stockholders’ Equity Requirement by that date, and, on November 20, 2023, the Staff formally notified the Company that it would move to delist the Company’s securities from Nasdaq unless the Company timely requested a hearing before the Nasdaq Hearings Panel (the “Panel”). The Company submitted the request for a hearing before the Panel (the “Hearing”), which request stayed any further action by Nasdaq pending completion of the Hearing and the expiration of any extension that may be granted by the Panel to the Company.

Additionally, on September 27, 2023, we received a deficiency letter (the “Nasdaq Minimum-Bid Price Letter”) from the Staff of the Nasdaq Capital Market LLC, stating that the bid price of our common stock had closed below \$1.00 per share for 30 consecutive business days and that, therefore, we are not in compliance with Nasdaq Listing Rule 5550(a)(2) (the “Minimum-Bid Price Requirement”). We had a 180-calendar day grace period, through March 25, 2024, to regain compliance with the Minimum-Bid Price Requirement. The Company did not regain compliance with the Bid Price Rule by March 25, 2024, and, accordingly, on March 26, 2024, the Staff issued a delist determination with respect to the deficiency, as required by the Nasdaq Listing Rules.

The Hearing was held on February 15, 2024 and, by decision dated March 11, 2024, the Panel granted the Company’s request for an extension through May 20, 2024 to demonstrate compliance with the Stockholders’ Equity Requirement and the Bid Price Requirement. In order to timely evidence compliance with the minimum bid price requirement in particular, the Company must evidence a closing bid price of at least \$1.00 per share for a minimum of 10, though generally not more than 20, consecutive business days by May 20, 2024.

We intend to take all reasonable measures available to regain compliance under the Nasdaq Listing Rules and remain listed on The Nasdaq Capital Market. If our common stock were delisted from The Nasdaq Stock Market, it could severely limit the liquidity of our common stock and your ability to sell our securities on the secondary market. Delisting from The Nasdaq Capital Market could adversely affect our ability to raise additional financing through the public or private sale of equity securities, would significantly affect the ability of investors to trade our securities and would negatively affect the value and liquidity of our common stock. Delisting could also have other negative results, including the potential loss of confidence by employees, the loss of institutional investor interest and fewer business development opportunities. If our common stock is delisted from The Nasdaq Capital Market, the price of our common stock may decline and our common stock may be eligible to trade on the OTC Bulletin Board, another over-the-counter quotation system, or on the pink sheets where an investor may find it more difficult to dispose of their common stock or obtain accurate quotations as to the market value of our common stock. Further, if we are delisted, we would incur additional costs under requirements of state “blue sky” laws in connection with any sales of our securities. These requirements could severely limit the market liquidity of our common stock and the ability of our stockholders to sell our common stock in the secondary market.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$3,850,000 from time to time under this prospectus supplement. The amount of the net proceeds to us from this offering will depend upon the number of shares of our common stock sold and the price at which they are sold. There can be no assurance that we will be able to sell any shares under or fully utilize the sales agreement.

We may use any net proceeds from the sale of securities under this prospectus supplement for general corporate purposes and working capital requirements, which may include, among other things, the advancement of our product candidates to obtain regulatory approval from the FDA. As a result, our management will have broad discretion to allocate the net proceeds of this offering. Pending their ultimate use, we intend to invest the net proceeds in a variety of securities, including commercial paper, government and non-government debt securities and/or money market funds that invest in such securities.

DIVIDEND POLICY

We currently intend to retain all available funds and any future earnings to fund the growth and development of our business. We have never declared or paid any cash dividends on our capital stock. We do not intend to pay cash dividends on our common stock in the foreseeable future. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Any future determination to declare dividends will be made at the discretion of our Board and will depend on our financial condition, operating results, capital requirements, general business conditions, and other factors that our Board may deem relevant.

DILUTION

Purchasers of the securities offered by this prospectus supplement will suffer immediate and substantial dilution in the net tangible book value per share of the common stock they purchase. Net tangible book value per share represents the amount of total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding as of December 31, 2023. Our net tangible book value as of December 31, 2023 was approximately \$0.7 million, or \$1.92 per share of our common stock.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers in this offering and the net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of all of the common stock in this offering at an assumed public offering price of \$4.40, which was the last reported sales price of our common stock on the Nasdaq Capital Market on May 8, 2024, and after deducting the estimated placement agent fees and the estimated expenses payable by us, but excluding the issuance of shares of common stock issuable to Fortress pursuant to the Founders Agreement, following the completion of this offering, our net tangible book value as of December 31, 2023 would have been approximately \$4.2 million, or \$3.46 per share of common stock. This represents an immediate increase in net book value of \$1.54 per share to our existing stockholders and an immediate dilution in net tangible book value of \$0.94 per share to new investors participating in this offering.

The following table illustrates this calculation on a per share basis:

Assumed public offering price per share of common stock	\$	4.40
Net tangible book value per share as of December 31, 2023	\$	1.92
Increase in net tangible book value per share attributable to investors participating in this offering	\$	1.54
As-adjusted net tangible book value per share as of December 31, 2023, after giving effect to this offering	\$	3.46
Dilution in net tangible book value per share to investors participating in this offering	\$	0.94

The table above assumes for illustrative purposes that an aggregate of 875,000 shares of our common stock are sold pursuant to this prospectus supplement at a price of \$4.40 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on May 8, 2024, for aggregate gross proceeds of \$3.9 million. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price, assuming all of our common stock in the aggregate amount of \$4.7 million is sold at that price, would result in an adjusted net tangible book value per share after the offering of \$4.16 per share and would increase the dilution in net tangible book value per share to new investors in this offering, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price to \$4.40 per share, assuming all of our common stock in the aggregate amount of \$3.0 million is sold at that price, would result in an adjusted net tangible book value per share after the offering of \$2.76 per share and an immediate decrease in net tangible book value of \$0.64 per share to new investors in this offering, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The number of shares of common stock to be outstanding after this offering is based on 341,147 shares of our common stock outstanding as of December 31, 2023, and excludes:

- 2,386,418 shares of common stock issuable upon exercise of outstanding warrants having a weighted-average exercise price of \$9.22 per share;
- 1,311 shares of common stock issuable upon the vesting and settlement of outstanding restricted stock award/units;
- 44,701 shares of common stock reserved for issuance and available for future grant under our 2015 Incentive Plan;
- 22,474 shares of common stock issuable upon the exercise of stock options with a weighted-average exercise price of \$85.50 per share;
- 223 shares of common stock issuable upon conversion of the Class A Preferred Stock, at the holders' election;
- 86,541 shares of common stock issuable upon the rounding up of fractional shares in connection with the reverse split that became effective on April 26, 2024;
- 51,469 shares of common stock issuable to Fortress pursuant to the Founders Agreement for warrant exercises and the annual PIK dividend; and
- 21,875 shares of common stock issuable to Fortress pursuant to the Founders Agreement following the closing of this offering.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding stock options or warrants and no settlement of the restricted stock units described above. 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 could result in further dilution to our stockholders. See "Risk Factors" beginning on page [S-10](#) of this prospectus supplement.

PLAN OF DISTRIBUTION

We entered into the sales agreement with Wainwright on May 10, 2024, under which we may issue and sell shares of our common stock having an aggregate gross sales price of up to \$3,850,000 from time to time through or to Wainwright acting as sales agent or principal.

Upon delivery of a placement notice and subject to the terms and conditions of the sales agreement, Wainwright may offer and sell shares of our common stock by any method permitted by law deemed to be an “at-the-market” offering as defined in Rule 415 promulgated under the Securities Act, including sales made directly on or through the Nasdaq Capital Market, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, directly to Wainwright as principal, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or in any other method permitted by law. We or Wainwright may suspend the offering of common stock upon notice and subject to other conditions.

We will pay Wainwright commissions, in cash, for its services in acting as agent in the sale of our common stock. Wainwright will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share sold. Because there is no minimum offering amount required as a condition of this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We have also agreed to reimburse Wainwright for certain specified expenses in an amount up to \$50,000, in addition to up to \$2,500 per due diligence update session for Wainwright’s counsel’s fees. We estimate that the total expenses for the offering, excluding compensation and reimbursements payable to Wainwright under the terms of the sales agreement, will be approximately \$125,000.

Settlement for sales of shares of common stock will occur on the second trading day following the date on which any sales are made (and on and after May 28, 2024 (or such later date on which the Securities and Exchange Commission’s final rule with respect to the shortening of the securities transaction settlement cycle becomes effective), on the first trading day following the date on which any sales are made), or on some other date that is agreed upon by us and Wainwright in connection with a particular transaction, in return for payment of the net proceeds to us. Sales of our common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Wainwright may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Wainwright will use its commercially reasonable efforts, consistent with its sales and trading practices, to solicit offers to purchase the shares of common stock under the terms and subject to the conditions set forth in the sales agreement. In connection with the sale of the shares of common stock on our behalf, Wainwright will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Wainwright will be deemed to be underwriting commissions or discounts. We have agreed to provide indemnification and contribution to Wainwright against certain civil liabilities, including liabilities under the Securities Act.

This offering of shares of our common stock pursuant to the sales agreement will terminate upon termination of the sales agreement as permitted therein. We and Wainwright may each terminate the sales agreement as provided therein.

To the extent required by Regulation M, Wainwright will not engage in any market making activities involving our common stock while the offering is ongoing under this prospectus supplement. Wainwright and its affiliates may in the future provide various investment banking, commercial banking and other financial services for us and our affiliates, for which services they may in the future receive customary fees.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement is filed with the SEC and is incorporated by reference into the registration statement of which this prospectus supplement is a part. See “*Where You Can Find More Information; Incorporation by Reference*” above.

This prospectus supplement in electronic format may be made available on a website maintained by Wainwright, and Wainwright may distribute this prospectus supplement electronically.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Troutman Pepper Hamilton Sanders LLP, Charlotte, North Carolina. The Agent is being represented in connection with this offering by Ellenoff Grossman & Schole LLP, New York, New York.

EXPERTS

The consolidated financial statements of Avenue Therapeutics, Inc. as of December 31, 2023 and December 31, 2022 and for each of the years then ended, have been incorporated by reference herein and in the registration statement in reliance on the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. The audit report covering the December 31, 2023 consolidated financial statements contains an explanatory paragraph that states the Company has incurred substantial operating losses since its inception and expects to continue to incur significant operating losses for the foreseeable future that raise substantial doubt about the Company's ability to continue as a going concern. The consolidated financial statements do not include any adjustments that might result from the outcome of that uncertainty.

WHERE YOU CAN FIND MORE INFORMATION

We file reports and proxy statements with the SEC. These filings include our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and proxy statements on Schedule 14A, as well as any amendments to those reports and proxy statements, which are available free of charge through our website as soon as reasonably practicable after we file them with, or furnish them to, the SEC. Our Internet website address is www.avenuetx.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. You should not rely on any such information in making your decision whether to purchase our securities. The SEC also maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding us and other issuers that file electronically with the SEC.

This prospectus supplement is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus supplement in accordance with the rules of the SEC. For more detail about us and any securities that may be offered by this prospectus supplement, you may examine the registration statement of which this prospectus supplement forms a part, including its exhibits and schedules. Statements contained in this prospectus supplement and the accompanying base prospectus as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” into this prospectus the information we file with the SEC in other documents, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. 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 such information. We incorporate by reference the documents listed below and any future information filed (rather than furnished) with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act between the date of this prospectus and the date all securities to which this prospectus relates have been sold or the offering is otherwise terminated and also between the date of the initial registration statement and prior to effectiveness of the registration statement, provided, however, that we are not incorporating any information furnished under Item 2.02 or Item 7.01 of any Current Report on Form 8-K:

- our Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC on [March 18, 2024](#); and
- our Current Reports on Form 8-K filed with the SEC on [January 8, 2024](#), [January 12, 2024](#), [February 23, 2024](#), [March 8, 2024](#), [March 15, 2024](#), [March 29, 2024](#), [April 26, 2024](#) and [May 1, 2024](#).

We will furnish without charge to you a copy of any or all of the documents incorporated by reference, including exhibits to these documents, upon written or oral request. Direct your written request to: Corporate Secretary, Avenue Therapeutics, Inc., 1111 Kane Concourse, Suite 301, Bay Harbor Islands, Florida 33154, or (781) 652-4500.

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

\$30,000,000



**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 \$30,000,000; however, as of the date of this prospectus, under the limitations described below, we are currently only eligible to sell approximately \$2,300,000 of securities. 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 December 3, 2021, the per share closing price of our common stock as reported on the Nasdaq Capital Market was \$1.31 per share.

The aggregate market value of our outstanding common stock held by non-affiliates is approximately \$16,000,000, which was calculated in accordance with General Instruction I.B.6 of Form S-3, based on 18,992,498 shares of common stock outstanding, of which 9,017,340 are held by non-affiliates, at the closing share price of \$1.78 on November 5, 2021, which was the highest closing price of our common stock reported on the NASDAQ Capital Market within the last 60 days prior to the date of this filing.

In this prospectus we are offering up to \$30,000,000 of securities; however, pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell the securities described in this prospectus in a public primary offering with a value exceeding more than one-third of the aggregate market value of our common stock held by non-affiliates in the twelve month period prior to the date of the sale of any such securities, so long as the aggregate market value of our outstanding common stock held by non-affiliates remains below \$75.0 million. As of the date of this prospectus, under such rules and including our prior sales within the twelve month period, we are only eligible to sell up to approximately \$2,300,000, of securities, until our circumstances, as described, change.

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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 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 _____, 2021

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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. This prospectus provides you with a general description of the securities offered by us. Each time we sell securities, we will provide a 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.

You should rely only on the information contained or incorporated by reference in this prospectus and any prospectus supplement or issuer free writing prospectus relating to a particular offering. No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus, any accompanying prospectus supplement and any related issuer free writing prospectus in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement nor any related issuer free writing prospectus shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. You should read the entire prospectus and any prospectus supplement and any related issuer free writing prospectus, as well as the documents incorporated by reference into this prospectus or any prospectus supplement or any related issuer free writing prospectus, before making an investment decision. Neither the delivery of this prospectus or any prospectus supplement or any issuer free writing prospectus nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement or issuer free writing prospectus is correct as of any date subsequent to the date hereof or of such prospectus supplement or issuer free writing prospectus, as applicable.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

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.

We are a specialty pharmaceutical company that seeks to develop and commercialize our product principally for use in the acute/intensive care hospital setting. Our current product candidate is intravenous (“IV”) Tramadol, for the treatment of post-operative acute pain. Under the terms of certain agreements described herein, we have an exclusive license to develop and commercialize IV Tramadol in the United States. In 2016, we completed a pharmacokinetic study for IV Tramadol in healthy volunteers as well as an end of phase 2 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. In December 2019, we submitted a New Drug Application (“NDA”) for IV Tramadol and received a Complete Response Letter (the “First CRL”) from the FDA in October 2020. In February 2021, we resubmitted the NDA for IV Tramadol. The FDA assigned a Prescription Drug User Fee Act (“PDUFA”) goal date of April 12, 2021 for the resubmitted NDA for IV Tramadol. On June 14, 2021, we announced that we had received a second Complete Response Letter (the “Second CRL”) from the FDA regarding our NDA for IV tramadol. We continue to pursue regulatory approval for IV Tramadol and had a Type A meeting with the FDA in July 2021. We submitted a formal dispute resolution request (“FDRR”) with the Office of Neuroscience of the FDA on July 27, 2021. On August 26, 2021, we received an Appeal Denied Letter from the Office of Neuroscience of the FDA in response to the FDRR submitted on July 27, 2021. On August 31, 2021, we submitted a FDRR with the Office of New Drugs (“OND”) of the FDA. On October 21, 2021, we received a written response from the OND of the FDA stating that the OND needs additional input from an Advisory Committee in order to reach a decision on the FDRR. A joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee is tentatively scheduled for February 15, 2022. 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 candidate.

On November 12, 2018, we entered into a Stock Purchase and Merger Agreement (“SPMA”) with InvaGen Pharmaceuticals Inc. (“InvaGen”), and Madison Pharmaceuticals, Inc. pursuant to which we agreed to sell the Company in a two-stage transaction. In the first stage, InvaGen agreed to purchase, for \$35 million, common shares representing 33.3% of the fully diluted capitalization of the Company. In the second stage, InvaGen would acquire the remaining issued and outstanding capital stock of the Company for approximately \$180 million in a reverse subsidiary merger transaction (the “Merger Transaction”). The SPMA was approved by a majority of our stockholders, including a majority of its non-affiliated stockholders, at its special shareholder meeting on February 6, 2019. On February 8, 2019, InvaGen acquired 5,833,333 shares of the Company’s common stock at \$6.00 per share (the “Stock Purchase Transaction”) for net proceeds of \$31.5 million after deducting commission fees and other offering costs, representing a 33.3% stake in the Company’s capital stock on a fully diluted basis.

Consummation of the Merger Transaction was conditioned upon, among other things, FDA approval of IV Tramadol, its labeling and scheduling, and the absence of certain other restrictions in effect with respect to IV Tramadol. Pursuant to the SPMA, if FDA approval of IV Tramadol was not obtained on or before April 30, 2021, InvaGen would not be subject to the mandatory closing obligations set forth in the SPMA with respect to the Merger Transaction (but would instead retain an option to complete the Merger Transaction up until such time as the SPMA was terminated). Pursuant to the SPMA, we could choose to terminate the SPMA after October 31, 2021, if FDA approval of IV Tramadol had not occurred by such time. On November 1, 2021, we terminated the SPMA.

Even though the SPMA has been terminated, InvaGen retains certain rights pursuant to the Stockholders Agreement, entered into on November 12, 2018 between us, InvaGen and Fortress, and other agreements entered into in connection therewith on such date. These rights exist as long as InvaGen maintains at least 75% of the common shares acquired in the Stock Purchase Transaction and include among other things, the right to restrict us from certain equity issuances and changes to our capital stock without obtaining InvaGen’s prior written consent.

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.

Our principal executive offices are located at 1140 Avenue of the Americas, Floor 9, New York, New York 10036, and our telephone number is 781-652-4500. We maintain a website on the Internet at www.avenuetx.com and our e-mail address is 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”).

RISK FACTORS

An investment in our securities involves a high degree of risk. The prospectus supplement applicable to each offering of our securities will contain a discussion of the risks applicable to an investment in our securities. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. Each of the referenced risks and uncertainties could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

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 regulatory approval from the FDA for our product candidate, our ability to obtain capital and achieve profitability, our ability to develop and commercialize our product candidate, our ability to obtain, perform under and maintain financing and strategic agreements and relationships, our ability to 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, our ability to adapt with the COVID-19 outbreak and its potential impact on our employees' and consultants' ability to complete work in a timely manner and our ability to obtain and adequately protect intellectual property rights for our product candidate.

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. The forward-looking statements contained in this prospectus reflect our views and assumptions only as of the date of this prospectus. Except as required by law, we assume no responsibility for updating any forward-looking statements. We qualify all of our forward-looking statements by these cautionary statements. In addition, with respect to all of our forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement, the net proceeds from the sale of securities offered by this prospectus will be used for general corporate purposes and working capital requirements, which may include, among other things, the advancement of our product candidate to obtain regulatory approval from the FDA, and in the event of FDA approval of our product candidate, towards the milestone payments due to our licensor and supplier upon FDA approval of our product candidate. We have not determined the amounts we plan to spend on the areas listed above or the timing of these expenditures, and we have no current plans with respect to acquisitions as of the date of this prospectus. As a result, unless otherwise indicated in the prospectus supplement, our management will have broad discretion to allocate the net proceeds of the offerings. Pending their ultimate use, we intend to invest the net proceeds in a variety of securities, including commercial paper, government and non-government debt securities and/or money market funds that invest in such securities.

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 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 Amended and Restated 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 December 3, 2021, there were 18,992,498 shares of our common stock outstanding held by 38 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 January 1 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. This PIK Dividend was waived in connection with the Waiver Agreement signed on November 12, 2018 between Avenue, Fortress and InvaGen.

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).

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 December 3, 2021, there were 14,951 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.

Any public offering 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 of Avenue Therapeutics, Inc. as of December 31, 2020 and 2019 and for each of the two years in the period ended December 31, 2020 incorporated by reference in this Prospectus and in the Registration Statement have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting. The report on the financial statements contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

WHERE YOU CAN FIND MORE INFORMATION

We are a public company and 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. 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. 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 which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus and accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus and accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. This prospectus incorporates 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, 2020 filed with the SEC on March 31, 2021](#);
- b) Our Quarterly Reports on Form 10-Q for the quarters ended September 30, 2021, filed with the SEC on [November 15, 2021](#), June 30, 2021, filed with the SEC on [August 16, 2021](#), and March 31, 2021, filed with the SEC on [May 17, 2021](#); and
- c) Our Current Reports on Form 8-K filed with the SEC on [January 8, 2021](#), [February 16, 2021](#), [March 1, 2021](#), [April 5, 2021](#), [May 3, 2021](#), [June 14, 2021](#), [July 15, 2021](#), [July 29, 2021](#), [August 27, 2021](#), [September 1, 2021](#), [September 3, 2021](#), [September 21, 2021](#), [October 25, 2021](#), [November 4, 2021](#), and [November 10, 2021](#).

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.



**Up to \$3,850,000
Common Stock**

PROSPECTUS SUPPLEMENT

H.C. Wainwright & Co.

May 10, 2024