

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

FORM S-3
REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

AVENUE THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

47-4113275
(I.R.S. Employer
Identification No.)

1111 Kane Concourse, Suite 301
Bay Harbor Islands, FL
(781) 652-4500
(Address, including zip code, and telephone number,
including area code, of registrant's principal executive
offices)

33154
(Zip Code)

Alexandra MacLean, M.D.
Chief Executive Officer
1111 Kane Concourse, Suite 301
Bay Harbor Islands, Florida 33154
(781) 652-4500
(Name, address, including zip code, and telephone number,
including area code, of agent for service)

Copies to:

Rakesh Gopalan
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201 N. Tryon Street, Suite 3000
Charlotte, NC 28202

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

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

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

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

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

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

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

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

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

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

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

Subject To Completion, Dated January 24, 2024

Preliminary Prospectus



33,080,598 Shares of Common Stock

This prospectus relates to the resale by the selling stockholders (the "Selling Stockholders") identified in this prospectus under the section "The Selling Stockholders," or their pledgees, donees, transferees or other successors in interest, from time to time, of shares of our Common Stock, par value \$0.0001 per share ("Common Stock"), comprised of (i) 16,540,299 shares of Common Stock (the "Series A Warrant Shares") issuable upon the exercise of our outstanding Series A Warrants to purchase Common Stock (the "Series A Warrants") and (ii) 16,540,299 shares of Common Stock (the "Series B Warrant Shares") issuable upon exercise of our outstanding Series B Warrants to purchase Common Stock (the "Series B Warrants" and together with the Series A Warrants, the "Warrants"). The Warrants were issued to the Selling Stockholders in a private placement transaction (the "Private Placement") which closed on January 9, 2024. For additional information about the Private Placement, see "Private Placement." We are registering the offer and sale of the shares of Common Stock issuable upon exercise of the Warrants (the "Warrant Shares") on behalf of the Selling Stockholders to satisfy certain registration rights that we have granted to the Selling Stockholders.

The Series A Warrants and Series B Warrants have an exercise price of \$0.3006 per share. The Series A Warrants are exercisable beginning on the date that we file a certificate of amendment to our charter to increase the number of authorized shares of Common Stock that we are permitted to issue under our Third Amended and Restated Certificate of Incorporation, as amended (the "Certificate of Incorporation"), to permit the exercise in full of the Warrants (the "Stockholder Approval Date") until the five-year anniversary of the Stockholder Approval Date. The Series B Warrants are exercisable on or after the Stockholder Approval date until the 18-month anniversary of the Stockholder Approval Date.

The Selling Stockholders may resell or dispose of the Warrant Shares, or interests therein, at fixed prices, at prevailing market prices at the time of sale or at prices negotiated with purchasers, to or through underwriters, broker-dealers, agents, or through any other means described in the section of this prospectus titled "Plan of Distribution." The Selling Stockholders will bear the costs of commissions and discounts, if any, attributable to the sale or disposition of the Warrant Shares, or interests therein, held by the Selling Stockholders. We will bear all costs, expenses and fees in connection with the registration of the offer and sale of the Warrant Shares under the Securities Act of 1933, as amended (the "Securities Act"). We will not receive any of the proceeds from the sale of the Warrant Shares by the Selling Stockholders. However, we will receive the proceeds of any cash exercise of the Warrants. See the section of this prospectus titled "Use of Proceeds" for more information.

The Common Stock is listed on The Nasdaq Capital Market under the symbol "ATXI." On January 23, 2024, the last reported sale price of our Common Stock was \$0.14 per share. You are urged to obtain current market quotations for our Common Stock.

Investing in our securities involves risks. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in this prospectus and under similar headings in the other documents that are incorporated by reference into this prospectus, as described on page 24 of this prospectus.

Neither the Securities and Exchange Commission (the "SEC") 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 , 2024

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This prospectus provides you with a general description of the Common Stock that may be resold by the Selling Stockholders. In certain circumstances, we may provide a prospectus supplement that will contain specific information about the terms of a particular offering by the Selling Stockholders. We also may provide a prospectus supplement to add information to, or update or change information contained in, this prospectus. To the extent there is a conflict between the information contained in this prospectus and any prospectus supplement, you should rely on the information in the 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 or any prospectus supplement — the statement in the later-dated document modifies or supersedes the earlier statement.

You should read both this prospectus and any applicable prospectus supplement together with the additional information about our company to which we refer you in the sections of this prospectus titled “*Where You Can Find More Information*” and “*Incorporation of Certain Documents by Reference*.” You should rely only on the information contained in or incorporated by reference into this prospectus and any prospectus supplement. Neither we nor the Selling Stockholders have authorized any dealer, salesperson or other person to provide you with different or inconsistent information. You should not assume that the information in this prospectus or any prospectus supplement is accurate as of any date other than the date on the front of those documents or that any document incorporated by reference is accurate as of any date other than its filing date. You should not consider this prospectus to be an offer or solicitation relating to the Common Stock in any jurisdiction in which such an offer or solicitation relating to the Common Stock is not authorized. Furthermore, you should not consider this prospectus to be an offer or solicitation relating to the Common Stock if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

Unless otherwise indicated, information contained or incorporated by reference in this 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 titled “*Risk Factors*.”

These and other factors could cause our future performance to differ materially from our assumptions and estimates. For investors outside the United States: we have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of our securities and the distribution of this prospectus outside the United States.

Unless the context indicates otherwise, when we refer to “Avenue,” “we,” “our,” “us” and the “Company” in this prospectus, we mean Avenue Therapeutics, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to “you,” we mean the potential holders of the applicable series of Common Stock.

This prospectus 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.

FORWARD-LOOKING STATEMENTS

This prospectus 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 integrate Baergic Bio, Inc. or develop BAER-101 or AJ201;
- 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 or unreliable;
- 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 voting majority of our common stock and has rights to receive significant share grants annually; and
- those risks discussed or referred to in “*Risk Factors*” elsewhere in this prospectus, as well as those described in any other filings which we make with the SEC.

Any forward-looking statements speak only as of the date on which they are made, and we undertake no obligation to publicly update or revise any forward-looking statements to reflect events or circumstances that may arise after the date of this prospectus, except as required by applicable law. Investors should evaluate any statements made by us in light of these important factors.

PROSPECTUS SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that may be important to you in making an investment decision. This summary is qualified in its entirety by the more detailed information included elsewhere in this prospectus and/or incorporated by reference herein. Before making your investment decision with respect to our securities, you should carefully read this entire prospectus, including the information in our filings with the SEC incorporated by reference into this prospectus.

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.

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 for the treatment of SBMA. The 12-week, multicenter, randomized, double-blind trial is enrolled approximately 25 patients, randomly assigned to AJ201 (600mg/day) or placebo. The primary endpoint of the study is to assess safety and tolerability of AJ201 in subjects with clinically and genetically defined SBMA. Secondary endpoints include pharmacodynamic data measuring change from baseline in mutant androgen receptor protein levels in skeletal muscle and changes in the fat and muscle composition as seen on MRI scans. Further details on the study can be found using the 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 OND in response to the 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.

Private Placement

On January 5, 2024, we entered into (i) an inducement offer letter agreement (the “January 2023 Investor Inducement Letter”) with a certain investor (the “January 2023 Investor”) in connection with certain outstanding warrants to purchase up to an aggregate of 1,940,299 shares of Common Stock, originally issued to the January 2023 Investor on January 31, 2023 (the “January 2023 Warrants”) and (ii) an inducement offer letter agreement (the “November 2023 Investor Inducement Letter Agreement” and, together with the January 2023 Investor Inducement Letter, the “Inducement Letters”) with certain investors (the “November 2023 Investors” and, together with the January 2023 Investor, the “Holders”) in connection with certain outstanding warrants to purchase up to an aggregate of 14,600,000 shares of Common Stock, originally issued to the November 2023 Investors on November 2, 2023 (the “November 2023 Warrants” and, together with the January 2023 Warrants, the “Existing Warrants”). The January 2023 Warrants had an exercise price of \$1.55 per share, and the November 2023 Warrants had an exercise price of \$0.3006 per share. The Holders are the Selling Stockholders identified in this prospectus under the section heading titled, “*The Selling Stockholders.*”

Pursuant to the Inducement Letters, (i) the January 2023 Investor agreed to exercise its January 2023 Warrants for cash at a reduced exercise price of \$0.3006 per share and (ii) the November 2023 Investors agreed to exercise their November 2023 Warrants for cash at the existing exercise price of \$0.3006, in each case in consideration for the Company’s agreement to issue in a private placement (x) Series A Warrants to purchase up to 16,540,299 shares of Common Stock and (y) Series B Warrants to purchase up to 16,540,299 shares of Common Stock.

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The transactions contemplated by the Inducement Letters closed on January 9, 2023 (the “Closing Date”). The Company received aggregate gross proceeds of approximately \$5.0 million from the exercise of the Existing Warrants by the Holders, before deducting placement agent fees and other expenses payable by the Company.

In the Inducement Letters, the Company agreed to file a registration statement providing for the resale of the New Warrant Shares. Accordingly, as required by the Inducement Letters, the registration statement of which this prospectus forms a part relates to the offer and resale of the Warrant Shares issuable to the Selling Stockholders upon the exercise of the Warrants.

Proposed Amendment to Certificate of Incorporation

As previously disclosed, effective January 9, 2024, the holders of a majority of the voting power of our capital stock executed a written consent (i) approving an increase in the number of the Company’s authorized shares of Common Stock from 75,000,000 to 200,000,000 (the “Authorized Share Increase”) through the filing of an amendment (the “Amendment”) to the Certificate of Incorporation with the Secretary of State of Delaware and (ii) authorizing, for purposes of complying with Nasdaq Listing Rule 5635(d), the issuance of shares of Common Stock underlying the Series A Warrants and the Series B Warrants in an amount equal to or in excess of 20% of the number of shares of Common Stock outstanding immediately prior to the issuance of such warrants (the “Share Issuance”). The written consent was signed by the holders of 3,133,886 shares of the Common Stock and 250,000 shares of the Company’s Class A Preferred Stock. Each share of Common Stock entitles the holder thereof to one vote on all matters submitted to stockholders and each share of Class A Preferred Stock has the voting power of 1.1 times (A) the number of outstanding shares of Common Stock plus (B) the whole shares of Common Stock into which the outstanding shares of Class A Preferred Stock are convertible, divided by the number of outstanding shares of Class A Preferred Stock, or 164.2 votes per share as of January 9, 2024. Accordingly, the holders of approximately 56.4% of the voting power of our capital stock as of January 9, 2024 signed the written consent approving the Authorized Share Increase, the Share Issuance and the Amendment. The Board also approved the Authorized Share Increase, the Share Issuance and the Amendment.

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.

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THE OFFERING

Issuer:	Avenue Therapeutics, Inc.
Securities Offered by Selling Stockholders:	33,080,598 shares of Common Stock issuable upon exercise of the Warrants.
Shares of Common Stock Outstanding Prior to this Offering:	27,720,368 shares as of January 4, 2024.
Shares of Common Stock Outstanding Assuming Exercise of All Warrants⁽¹⁾⁽²⁾:	70,385,966
Terms of the Offering	The Selling Stockholders will determine when and how they will sell the Common Stock offered in this prospectus, as described in the section of this prospectus titled “ <i>Plan of Distribution.</i> ”
Use of Proceeds:	We will not receive any proceeds from the sale of the Common Stock by the Selling Stockholders in this offering. However, we will receive the proceeds of any cash exercise of the Warrants. We intend to use the net proceeds from any cash of the Warrants for working capital and general corporate purposes. See “ <i>Use of Proceeds.</i> ”
Risk Factors:	See “ <i>Risk Factors</i> ” incorporated by reference into this prospectus from our most current Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q for a discussion of certain factors you should carefully consider before deciding to invest in shares of our Common Stock.
Nasdaq Capital Market Symbol:	ATXI

(1) The number of shares of Common Stock outstanding after this offering is based on 37,305,368 shares of our Common Stock outstanding as of January 5, 2024, and excludes:

· 22,803,719 shares of Common Stock issuable upon exercise of outstanding warrants having a weighted-average exercise price of \$0.53 per share;

- 6,955,299 shares of Common Stock issuable upon the exercise of certain warrants, but held in abeyance pursuant to the terms of such warrants;
 - 63,750 shares of Common Stock issuable upon the vesting and settlement of outstanding restricted stock units;
 - 3,352,489 shares of Common Stock reserved for issuance and available for future grant under our 2015 Incentive Plan;
 - 1,685,000 shares of Common Stock issuable upon the exercise of stock options with a weighted-average exercise price of \$1.14 per share; and
 - 16,666 shares of Common Stock issuable upon conversion of the Class A Preferred Stock, at the holders' election.
- (2) The number of shares of Common Stock outstanding after this offering also gives effect to the filing of the Amendment effecting the Share Increase.

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RISK FACTORS

Investing in our Common Stock involves a high degree of risk. Our business is influenced by many factors that are difficult to predict, involve uncertainties that may materially affect actual results and are often beyond our control. We have identified a number of these factors under the heading “*Risk Factors*” in our Annual Report on Form 10-K for the year ended December 31, 2022, as updated by our subsequently filed Quarterly Reports on Form 10-Q, each of which are incorporated by reference in this prospectus, as well as in other information included or incorporated by reference in this prospectus and any prospectus supplement. You should consider carefully these risks and uncertainties before deciding to invest in our Common Stock. If any of the risks identified as risk factors in the incorporated documents were to materialize, our business, financial condition, results of operations, and future growth prospects could be materially and adversely affected. In that event, the market price of our Common Stock could decline, and you could lose part of or all of your investment in our Common Stock. See the section of this prospectus titled “*Where You Can Find More Information.*”

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USE OF PROCEEDS

We will not receive any proceeds from the sale of the Warrant Shares covered by this prospectus and any accompanying prospectus supplement. All proceeds from the sale of the Warrant Shares will be for the respective accounts of the Selling Stockholders named herein. However, we will receive the proceeds of any cash exercise of the Warrants. We intend to use the net proceeds from any cash exercise of the Warrants for working capital and general corporate purposes.

We will bear all other costs, fees and expenses incurred in effecting the registration of the offering and sale of the Warrant Shares covered by this prospectus and any accompanying prospectus supplement, including, without limitation, all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants, in accordance with the terms of the Inducement Letters. The Selling Stockholders will pay any discounts, commissions, and fees of underwriters, selling brokers, dealer managers or similar securities industry professionals incurred by the Selling Stockholders in disposing of the Warrant Shares covered by this prospectus.

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THE PRIVATE PLACEMENT

On January 5, 2024, we entered into the Inducement Letters with the Holders in connection with the Existing Warrants. The January 2023 Warrants had an exercise price of \$1.55 per share, and the November 2023 Warrants had an exercise price of \$0.3006 per share.

Pursuant to the Inducement Letters, (i) the January 2023 Investor agreed to exercise its January 2023 Warrants for cash at a reduced exercise price of \$0.3006 per share and (ii) the November 2023 Investors agreed to exercise their November 2023 Warrants for cash at the existing exercise price of \$0.3006, in each case in consideration for the Company's agreement to issue in a private placement (x) the Series A Warrants and (y) the Series B Warrants. The Series A Warrants and the Series B Warrants were issued on January 9, 2024 (the “Closing Date”). We received aggregate gross proceeds of approximately \$5.0 million from the exercise of the Existing Warrants, before deducting placement agent fees and other offering expenses payable by us.

Pursuant to the Inducement Letters, we agreed to file a registration statement on Form S-3 providing for the resale of the Warrant Shares within 30 days of the date of the Inducement Letters, and to use best efforts to cause such registration statement to be declared effective by the SEC within 90 days following the date of the Inducement Letters and to keep such registration statement effective at all times until the Holders no longer own any Warrants or Warrant Shares. We have filed the registration statement of which this prospectus forms a part pursuant to the Inducement Letters.

The Company engaged Maxim Group LLC (“Maxim”) to act as its exclusive financial advisor and warrant solicitation agent in connection with the transactions summarized above and has agreed to pay Maxim a cash fee equal to 3.5% of the gross proceeds of the exercise price paid for the January 2023 Warrants and 7.0% of the gross proceeds of the exercise price paid for the November 2023 Warrants. The Company also agreed to reimburse Maxim for its expenses in connection with the exercise of the Existing Warrants and the issuance of the New Warrants in an aggregate amount of up to \$15,000.

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THE SELLING STOCKHOLDERS

We have prepared this prospectus to allow the Selling Stockholders or certain of their pledgees, donees, transferees or other successors in interest to sell or otherwise dispose of, from time to time, the Warrant Shares issuable upon exercise of the Warrants.

The Warrants held by the Selling Stockholders contain limitations which prevent the holder from exercising such Warrants if such exercise would cause any of the Selling Stockholders, together with certain related parties, to beneficially own a number of shares of Common Stock which would exceed 4.99% (or, at the election of the holder,

9.99%) of our then outstanding shares of Common Stock following such exercise, excluding for the purposes of such determination, shares of Common Stock issuable upon exercise of the Warrants which have not been exercised.

In connection with certain registration rights that we granted to the Selling Stockholders pursuant to the Inducement Letters, we filed with the SEC a registration statement on Form S-3, of which this prospectus forms a part, with respect to the resale or other disposition of the Warrant Shares offered by this prospectus from time to time on Nasdaq, in privately negotiated transactions or otherwise. We have agreed to prepare and file amendments and supplements to the registration statement to the extent necessary to keep the registration statement effective for the period of time required under our agreement with the Selling Stockholders.

All information with respect to the Selling Stockholders' ownership of the Warrant Shares has been furnished by or on behalf of the Selling Stockholders and is as of January 23, 2024. The percentage ownership data is based on 70,385,966 shares of Common Stock issued and outstanding as of January 5, 2024. We believe, based on information supplied by the Selling Stockholders, that except as may otherwise be indicated in the table below, the Selling Stockholders and their affiliates listed in any footnote to the table below have sole voting and dispositive power with respect to the Shares reported as beneficially owned by them.

The Selling Stockholders may sell some, all or none of the Warrant Shares. We do not know how long the Selling Stockholders will hold the Warrant Shares before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale or other disposition of any of the Warrant Shares. The Warrant Shares may be offered and sold from time to time by the Selling Stockholders pursuant to this prospectus.

Because the Selling Stockholders may sell some or all of the Warrant Shares included in this prospectus, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the Common Stock, no estimate can be given as to the number of Warrant Shares available for resale hereby that will be held by the Selling Stockholders in the future. In addition, the Selling Stockholders may have sold, transferred or otherwise disposed of, or may sell, transfer or otherwise dispose of, at any time and from time to time, the Warrant Shares it holds in transactions exempt from the registration requirements of the Securities Act after the date on which they provided the information set forth in the table below. We have, therefore, assumed for the purposes of the following table, that the Selling Stockholders will sell all of the Warrant Shares beneficially owned by them and their affiliates listed in any footnote to the table below that are covered by this prospectus.

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Selling Stockholders Information:

Name of Selling Stockholder ⁽¹⁾	Shares Beneficially Owned Immediately Prior to the Offering	Warrant Shares Being Offered for Resale Under this Prospectus ⁽¹⁾	Number of Shares Beneficially Owned After Sale of Warrant Shares ⁽²⁾	Percentage of Outstanding Shares of Common Stock Beneficially Owned Immediately Following the Sale of Warrant Shares ⁽³⁾⁽⁴⁾
Armistice Capital, LLC ⁽⁵⁾	19,212,100 ⁽⁶⁾	25,900,000	19,212,100	27.3%
Bigger Capital Fund, LP ⁽⁷⁾	961,350 ⁽⁸⁾	1,650,000	961,350	1.4%
District 2 Capital Fund LP ⁽⁹⁾	1,361,350 ⁽¹⁰⁾	1,650,000	1,361,350	1.9%
Sabby Volatility Warrant Master Fund, Ltd. ⁽¹¹⁾	4,900,602 ⁽¹²⁾	3,880,598	4,900,602	7.0%

* Less than 1%

- (1) The Warrants are subject to a beneficial ownership limitation of 4.99% (or, at the election of the holder, 9.99%) (the "Beneficial Ownership Limitation"), which limitation precludes each Selling Stockholder from exercising any portion of its Warrants to the extent that, following such exercise, such Selling Stockholder's ownership of our Common Stock would exceed the Beneficial Ownership Limitation.
- (2) Assumes the Selling Stockholders sell all of the Warrant Shares being offered by this prospectus.
- (3) Percentage calculated based upon the assumption that the Selling Stockholders sell all of the Warrant Shares offered by this prospectus.
- (4) The amounts and percentages in the table are provided without regard to the applicable Beneficial Ownership Limitation.
- (5) The securities are directly held by Armistice Capital Master Fund Ltd., a Cayman Islands exempted company (the "Master Fund"), and may be deemed to be beneficially owned by: (i) Armistice Capital, LLC ("Armistice Capital"), as the investment manager of the Master Fund; and (ii) Steven Boyd, as the Managing Member of Armistice Capital. The address of Armistice Capital Master Fund Ltd. is c/o Armistice Capital, LLC, 510 Madison Avenue, 7th Floor, New York, NY 10022.
- (6) Consists of: (i) registered warrants to purchase 13,622,100 share of Common Stock, subject to the Beneficial Ownership Limitation; (ii) 2,866,000 shares of Common Stock; and (iv) 2,684,000 shares of Common Stock currently held in abeyance pursuant to the Beneficial Ownership Limitation.
- (7) Michael Bigger, Managing Member of Bigger Capital GP, LLC, General Partner of Bigger Capital Fund, LP, has discretionary authority to vote and dispose of the shares held by Bigger Capital Fund, LP and may be deemed to be the beneficial owner of these shares. The address of Bigger Capital Fund, LP is 11700 W Charleston Blvd 170-659, Las Vegas, NV 89135.
- (8) Consists of warrants to purchase 961,350 shares of Common Stock, subject to the Beneficial Ownership Limitation.
- (9) Michael Bigger, Managing Member of District 2 GP LLC, General Partner of District 2 Capital Fund LP, has discretionary authority to vote and dispose of the shares held by District 2 Capital Fund LP and may be deemed to be the beneficial owner of these shares. The address of District 2 Capital Fund, LP is 14 Wall Street, 2nd Floor, Huntington, NY 11743.
- (10) Consists of: (i) warrants to purchase 961,350 shares of Common Stock, subject to the Beneficial Ownership Limitation and (ii) 400,000 shares of Common Stock.
- (11) Sabby Management, LLC, the investment manager to Sabby Volatility Warrant Master Fund, Ltd. ("Sabby"), has discretionary authority to vote and dispose of the shares held by Sabby and may be deemed to be the beneficial owner of these shares. Hal Mintz ("Mr. Mintz"), in his capacity as manager of Sabby Management, LLC, may also be deemed to have investment discretion and voting power over the shares held by Sabby. Sabby Management, LLC and Mr. Mintz each disclaim any beneficial ownership of these shares.
- (12) Consists of: (i) warrants to purchase 2,787,800 shares of Common Stock, subject to the Beneficial Ownership Limitation; (ii) 1,662,503 shares of Common Stock; and (iii) 490,299 shares of Common Stock held in abeyance pursuant to the Beneficial Ownership Limitation.

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DESCRIPTION OF SECURITIES BEING REGISTERED

Avenue Therapeutics has one class of securities registered under Section 12 of the Securities Act of 1934, as amended: our Common Stock. The following description

of our Common Stock is a summary and is qualified in its entirety by reference to our Certificate of Incorporation, and our Second Amended and Restated Bylaws (the "Bylaws"). We encourage you to read the Certificate of Incorporation and Bylaws as well as the applicable provisions of the General Corporation Law of the State of Delaware, as amended (the "DGCL"), for more information.

Authorized Capital Stock

Our authorized capital stock consists of 75,000,000 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. After giving effect to the filing of the Amendment with the Secretary of State of the State of Delaware, our authorized capital stock will consist of 200,000,000 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 will be designated as Class A Preferred Stock and the remainder of which will be undesignated Preferred Stock.

As of January 5, 2024, there were 37,305,368 shares of our Common Stock outstanding held by 31 record stockholders.

Common Stock

Voting Rights

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. However, the holders of our outstanding Class A Preferred Stock, which is held exclusively by Fortress, are entitled to cast, for each share of Class A Preferred Stock, the number of votes that is equal to 1.1 times a fraction, the numerator of which is the sum of (A) the aggregate number of shares of outstanding Common Stock and (B) the whole shares of Common Stock into which the shares of outstanding Class A Preferred Stock are convertible and the denominator of which is the aggregate number of shares of outstanding Class A Preferred Stock. Thus, Fortress, so long as it holds all shares of our Class A Preferred Stock, will at all times have voting control of us. Further, for a period of ten years from the date of the first issuance of shares of Class A Preferred Stock, the holders of record of the shares of Class A Preferred Stock (or other capital stock or securities issued upon conversion of or in exchange for the Class A Preferred Stock), exclusively and as a separate class, are entitled to appoint or elect the majority of our directors, however, the Company and Fortress have historically elected to waive application of this provision of the certificate of incorporation, and instead the holders of the Common Stock have voted together with the holders of the Class A Preferred Stock for all directors at our annual meetings of stockholders, with the holders of the Class A Preferred Stock utilizing the supervoting rights described above.

Liquidation and Other Rights

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.

Listing

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.

Dividends

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. Pursuant to the certificate of designation relating to the series A preferred stock, we are prohibited from paying dividends on our Common Stock until all dividends required to be paid to the holders of our Class A Preferred Stock have been paid or declared and set apart for payment.

Anti-Takeover Effects of Various Provisions of Delaware Law and Avenue Therapeutics' Certificate of Incorporation and Bylaws

Provisions of the DGCL and our Certificate of Incorporation and Bylaws could make it more difficult to acquire Avenue Therapeutics by means of a tender offer, a proxy contest or otherwise, or to remove incumbent officers and directors. These provisions, including those summarized below, may encourage certain types of coercive takeover practices and takeover bids.

Delaware Anti-Takeover Statute. In general, Section 203 of the DGCL prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years following the time the person became an interested stockholder, unless the business combination or the acquisition of shares that resulted in a stockholder becoming an interested stockholder is approved in a prescribed manner. Generally, a "business combination" includes a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns (or within three years prior to the determination of interested stockholder status did own) 15% or more of a corporation's voting stock. However, our Certificate of Incorporation provides that we are not subject to the anti-takeover provisions of Section 203 of the DGCL.

Removal. Subject to the rights of any holders of any outstanding series of our Preferred Stock, stockholders may remove our directors with or without cause. Removal will require the affirmative vote of holders of a majority of our voting stock.

Size of Board and Vacancies. Our Bylaws provide that the number of directors be fixed exclusively by the board of directors. Any vacancies created on its board of directors resulting from any increase in the authorized number of directors or the death, resignation, retirement, disqualification, removal from office or other cause will be filled by a majority of the board of directors then in office, even if less than a quorum is present, or by a sole remaining director. Any director appointed to fill a vacancy on our board of directors will be appointed until the next annual meeting and until his or her successor has been elected and qualified.

Requirements for Advance Notification of Stockholder Nominations and Proposals. Our Bylaws establish advance notice procedures with respect to stockholder proposals and nomination of candidates for election as directors other than nominations made by or at the direction of its board of directors or a committee of our board of directors.

Undesignated Preferred Stock. Our board of directors is authorized to issue up to 2,000,000 shares of preferred stock without additional stockholder approval, which preferred stock could have voting rights or conversion rights that, if exercised, could adversely affect the voting power of the holders of Common Stock. The issuance of shares of preferred stock may have the effect of delaying, deferring or preventing a change in control of the Company without any action by the Company's stockholders.

Limitation on Liability of Directors and Indemnification of Directors and Officers

Elimination of Liability of Directors. The DGCL authorizes corporations to limit or eliminate the personal liability of directors to corporations and their stockholders for

monetary damages for breaches of directors' fiduciary duties as directors, and our Certificate of Incorporation includes such an exculpation provision. Our Certificate of Incorporation provides that, to the fullest extent permitted by the DGCL, no director will be personally liable to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. While our Certificate of Incorporation provides directors with protection from awards for monetary damages for breaches of their duty of care, it does not eliminate this duty. Accordingly, our Certificate of Incorporation has no effect on the availability of equitable remedies such as an injunction or rescission based on a director's breach of his or her duty of care. The provisions apply to an officer of Avenue Therapeutics only if he or she is a director of Avenue Therapeutics and is acting in his or her capacity as director, and do not apply to officers of Avenue Therapeutics who are not directors. Additionally, our Certificate of Incorporation provides that, to the fullest extent permitted by law, we renounce any interest or expectancy in a transaction or matter that may be a corporate opportunity for us if it was presented to, or acquired, created or developed by, or which otherwise comes into the possession of, (i) any director on our board of directors who is not an employee of the Company or any of its subsidiaries, or (ii) any holder of our Class A Preferred Stock or any affiliate or other related person of any such holder, other than someone who is an employee of the Company or any of its subsidiaries, and no person shall have any duty to present such corporate opportunity to us and will not be liable to us for pursuing or acquiring such opportunity, or referring such opportunity to a third party.

Indemnification of Directors, Officers and Employees. Our Bylaws require us to indemnify any person who was or is a party or is threatened to be made a party to, or was otherwise involved in, a legal proceeding by reason of the fact that he or she is or was a director, officer or employee of Avenue Therapeutics or, while a director, officer or employee of Avenue Therapeutics, is or was serving in a fiduciary capacity with another enterprise (including any corporation, partnership, limited liability company, joint venture, trust, association or other unincorporated organization or other entity and any employee benefit plan, to the fullest extent authorized by the DGCL, as it exists or may be amended, against all expense, liability and loss (including attorneys' fees, judgments, fines, U.S. Employee Retirement Income Security Act of 1974, as amended, excise taxes or penalties and amounts paid in settlement by or on behalf of such person) actually and reasonably incurred in connection with such service. We are authorized under our Bylaws to carry directors' and officers' insurance protecting us, any director, officer or employee of ours or, against any expense, liability or loss, whether or not we have the power to indemnify the person under the DGCL. We may, to the extent authorized from time to time, indemnify any of our agents to the fullest extent permitted with respect to directors, officers and employees in our Bylaws.

The limitation of liability and indemnification provisions in our Certificate of Incorporation and Bylaws may discourage stockholders from bringing a lawsuit against our directors for breach of fiduciary duty. These provisions also may reduce the likelihood of derivative litigation against our directors and officers, even though such an action, if successful, might otherwise benefit us and our stockholders. By its terms, the indemnification provided for in our Bylaws is not exclusive of any other rights that the indemnified party may be or become entitled to under any law, agreement, vote of stockholders or directors, provisions of our Certificate of Incorporation or Bylaws or otherwise. Any amendment, alteration or repeal of our Bylaws' indemnification provisions is, by the terms of our Bylaws, prospective only and will not adversely affect the rights of any indemnity in effect at the time of any act or omission occurring prior to such amendment, alteration or repeal.

CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS

The following discussion summarizes certain U.S. federal income tax considerations of the acquisition, ownership and disposition of the Common Stock offered by this prospectus but does not purport to be a complete analysis of all potential tax effects. This discussion does not address effects of other U.S. federal tax laws, such as estate and gift tax laws, or of state, local, non-U.S or other tax considerations that may be relevant to a purchaser or holder of the Common Stock in light of their particular circumstances. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended (the "Code"), the Treasury regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the "IRS"), in each case as of the date hereof. These authorities may change, possibly with retroactive effect, or may be subject to differing interpretations that may adversely affect a holder of the Common Stock. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the acquisition, ownership and disposition of the Common Stock.

This discussion is limited to holders that hold the Common Stock as a capital asset within the meaning of Section 1221 of the Code (generally property held for investment). This discussion does not describe all of the U.S. federal income tax consequences that may be relevant to a holder in light of its particular circumstances, including the impact of the alternative minimum tax and of the Medicare contribution tax on net investment income. In addition, it does not address consequences for holders subject to special rules, including without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding the Common Stock as part of a hedge, straddle, conversion, or other integrated transaction;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- S corporations or entities or arrangements that are treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- real estate investment trusts or regulated investment companies;
- U.S. persons whose functional currency is not the U.S. dollar;
- persons subject to special tax accounting rules;
- persons who hold or receive the Common Stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- persons deemed to sell our Common Stock under the constructive sale provisions of the Code;
- tax-qualified retirement plans, individual retirement accounts or other tax-deferred accounts; and
- "qualified foreign pension funds" as defined in Section 897(l)(2) of the Code.

If a partnership (or any other entity treated as a partnership for U.S. federal income tax purposes) holds the Common Stock, the U.S. federal income tax treatment of a partner of that partnership generally will depend upon the status of the partner and the activities of the partnership. If you are a partnership or a partner of a partnership holding the Common Stock, you should consult your tax advisors as to the particular U.S. federal income tax consequences of holding and disposing of the Common Stock.

This discussion is for informational purposes only and is not tax advice. You should consult your own independent tax advisor concerning the application of the U.S. federal income tax laws to your particular circumstances as well as any tax consequences for the acquisition, ownership, or disposition of the Common Stock arising under other U.S. federal tax laws and the laws of any state, local or non-U.S. tax jurisdiction or under any applicable income tax treaty.

For purposes of this discussion, a “U.S. holder” is a beneficial owner of our Common Stock that, for U.S. federal income tax purposes, is or is treated as:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust that (i) is subject to the primary supervision of a U.S. court and the control of one or more “United States persons” (within the meaning of Section 7701(a)(30) of the Code) or (ii) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

A “non-U.S. holder” is any beneficial owner of our Common Stock that is not a U.S. holder.

U.S. Holders

Distributions in General

If distributions are made with respect to the Common Stock, such distributions will be treated as dividends to the extent of our current or accumulated earnings and profits as determined under the Code. Subject to customary conditions and limitations, dividends will be eligible for the dividends-received deduction in the case of U.S. holders that are (or are treated for U.S. federal income tax purposes) as corporations. Dividends paid to non-corporate U.S. holders generally will qualify for taxation at preferential rates if those holders meet certain holding period and other applicable requirements. Dividends received by non-corporate U.S. holders may also be subject to the additional 3.8% tax on net investment income. Any portion of a distribution that exceeds our current and accumulated earnings and profits will first be applied to reduce a U.S. holder’s tax basis in the Common Stock, but not below zero. Distributions in excess of our current and accumulated earnings and profits and in excess of a U.S. holder’s tax basis in its shares will be taxable as gain from the disposition of the Common Stock, the tax treatment of which is discussed below.

Extraordinary Dividends

Dividends that exceed certain thresholds in relation to a U.S. holder’s tax basis in the Common Stock could be characterized as “extraordinary dividends” under Section 1059 of the Code. Corporate U.S. holders that have held our Common Stock for two years or less before the dividend announcement date and that receive an extraordinary dividend will generally be required to reduce their tax basis in the stock by the nontaxed portion of the dividend due to the dividends-received deduction. If the amount of reduction exceeds the U.S. holder’s tax basis in the stock, the excess will be taxable as gain from the disposition of the stock, the tax treatment of which is discussed below. Non-corporate U.S. holders that receive an extraordinary dividend will be required to treat any losses on the sale of our Common Stock as long-term capital losses to the extent of the extraordinary dividends such U.S. holders receive that qualify for taxation as the preferential rates discussed above under “— *Distributions in General*.” U.S. holders are urged to consult their tax advisors with respect to the eligibility for and amount of any dividend received deduction and the application of Section 1059 of the Code to any dividends they receive.

Disposition of Common Stock by Sale, Exchange or Redemption

Upon any sale or disposition (other than certain redemptions, as discussed below) of the Common Stock, a U.S. holder generally will recognize capital gain or loss equal to the difference between the amount realized by the U.S. holder and the U.S. holder’s adjusted tax basis in the Common Stock. Such capital gain or loss will be long-term capital gain or loss if the U.S. holder’s holding period for the Common Stock is longer than one year. Non-corporate U.S. holders may be eligible for preferential tax rates on long-term capital gains but also may be subject to the additional 3.8% tax on net investment income. The deductibility of capital losses is subject to limitations.

A redemption of the Common Stock will be treated as a sale or exchange described in the preceding paragraph if the redemption, based on the facts and circumstances, is treated for U.S. federal income tax purposes as (i) a “complete termination” of your interest in the Common Stock, (ii) a “substantially disproportionate” redemption of your Common Stock, or (iii) is “not essentially equivalent to a dividend”, each within the meaning of Section 302 of the Code. In determining whether any of these tests has been met, you must take into account not only the Common Stock and other equity interests that you actually own but also other equity interests that you constructively own under U.S. federal income tax rules.

If you meet none of the alternative tests described above, the redemption will be treated as a distribution subject to the rules described under “— *Distributions In General*.” If a redemption of the Common Stock is treated as a distribution that is taxable as a dividend, you are urged to consult your tax advisor regarding the allocation of your tax basis as between the redeemed and remaining shares of Common Stock.

Information Reporting and Backup Withholding

We or an applicable withholding agent will report to our U.S. holders and the IRS the amount of dividends (including deemed dividends) paid during each year and the amount of any tax withheld with respect to the Common Stock. Certain non-corporate U.S. holders may be subject to U.S. backup withholding at a rate of 28% on payments of dividends on the Common Stock unless the holder furnishes the payor or its agent with a taxpayer identification number, certified under penalties of perjury, and certain other information or otherwise establishes an exemption from backup withholding. Backup withholding tax is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a U.S. holder’s U.S. federal income tax liability, provided the U.S. holder timely furnishes the required information to the IRS.

Non-U.S. Holders

Distributions

If distributions are made with respect to the Common Stock, such distributions will be treated as dividends to the extent of our current or accumulated earnings and profits as determined under the Code and may be subject to withholding as discussed below. Any portion of a distribution that exceeds our current and accumulated earnings and profits will first be applied to reduce the Non-U.S. holder’s basis in the Common Stock, but not below zero. If the distribution exceeds our current and accumulated earnings and profits and the Non-U.S. holder’s basis, the excess will be treated as gain from the disposition of the Common Stock, the tax treatment of which is discussed below.

In addition, if we are classified as a U.S. real property holding corporation (a “USRPHC”) within the meaning of Section 897(c) of the Code and any distribution exceeds our current and accumulated earnings and profits, we will need to satisfy our withholding requirements either by (a) treating the entire distribution (even if in excess of earnings and profits) as a dividend subject to the withholding rules described below and withhold at a minimum rate of 15% or such lower rate as may be specified by an applicable income tax treaty for distributions from a USRPHC; or (b) treating (i) only the amount of the distribution equal to our reasonable estimate of our current and accumulated earnings and profits as a dividend subject to the withholding rules in the following paragraph; and (ii) the excess portion of the distribution as subject to withholding at a rate of 15% (or such lower rate as may be specified by an applicable income tax treaty), as if such excess were the result of a sale of shares in a USRPHC, with a credit generally allowed against the Non-U.S. holder’s U.S. federal income tax liability for the tax withheld from such excess. We believe that we currently are not a USRPHC, and we do not expect to become a USRPHC for the foreseeable future (see discussion of USRPHCs below under “— *Disposition of Common Stock, Including Redemptions*”).

Dividends (including amounts distributed by a USRPHC and subject to withholding as dividends per the preceding paragraph) paid to a Non-U.S. holder of the Common Stock will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. However, dividends that are

treated as being effectively connected with the conduct of a trade or business by the Non-U.S. holder within the United States (and, where a tax treaty applies, are attributable to a permanent establishment maintained by the Non-U.S. holder in the United States) are not subject to this withholding tax, provided that certain certification and disclosure requirements are satisfied including completing IRS Form W-8ECI (or other applicable form). Instead, such dividends are subject to U.S. federal income tax on a net income basis in the same manner as if the Non-U.S. holder were a United States person (as defined under the Code), unless an applicable income tax treaty provides otherwise. Any such effectively connected dividends received by a foreign corporation may be subject to an additional “branch profits tax” at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

A Non-U.S. holder of the Common Stock who wishes to claim the benefit of an applicable treaty rate and avoid backup withholding for dividends, as discussed below, will be required to (i) complete IRS Form W-8BEN or Form W-8BEN-E (or other applicable form) and certify under penalty of perjury that such holder is not a United States person as defined under the Code and is eligible for treaty benefits, or (ii) if the Common Stock is held through certain foreign intermediaries, satisfy the relevant certification requirements of applicable Treasury regulations. A Non-U.S. holder of the Common Stock eligible for a reduced rate of U.S. withholding tax pursuant to an income tax treaty may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the U.S. Internal Revenue Service.

Disposition of Common Stock, Including Redemptions

Any gain realized by a Non-U.S. holder on the disposition of the Common Stock generally will not be subject to U.S. federal income or withholding tax unless:

- the gain is effectively connected with the conduct of a trade or business by the Non-U.S. holder in the United States (and, if required by an applicable income tax treaty, attributable to a permanent establishment maintained by the Non-U.S. holder in the United States);
- the Non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of disposition, and certain other conditions are met; or
- we are or have been a USRPHC, as defined in Section 897(c) of the Code, and a Non-U.S. holder owned directly or pursuant to applicable attribution rules at any time during the five-year period ending on the date of disposition more than 5% of the Common Stock — assuming that the Common Stock is regularly traded on an established securities market, within the meaning of Section 897(c)(3) of the Code.

A Non-U.S. holder described in the first bullet point immediately above will generally be subject to tax on the gain derived from the sale under regular graduated U.S. federal income tax rates in the same manner as if the Non-U.S. holder were a United States person as defined under the Code, and, if it is a corporation, may also be subject to branch profits tax equal to 30% (generally applicable to its effectively connected earnings and profits) or at such lower rate as may be specified by an applicable income tax treaty.

An individual Non-U.S. holder described in the second bullet point immediately above will be subject to a flat 30% tax (or at such reduced rate as may be provided by an applicable tax treaty) on the gain derived from the sale, which may be offset by U.S. source capital losses, even if the individual is not considered a resident of the United States for U.S. federal income tax purposes.

A Non-U.S. holder described in the third bullet point above will be subject to U.S. federal income tax under regular graduated U.S. federal income tax rates with respect to the gain realized in the same manner as if the Non-U.S. holder were a United States person as defined under the Code. A corporation is a USRPHC if it is a U.S. corporation and the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests and its other assets used or held for use in a trade or business. We believe that we currently are not a USRPHC for U.S. federal income tax purposes, and we do not expect to become a USRPHC for the foreseeable future. Our Common Stock is listed on the NASDAQ Capital Market and we believe that, for as long as we continue to be so listed, our Common Stock will be treated as regularly traded on an established securities market. However, if we become a USRPHC and our Common Stock is regularly traded on an established securities market, a Non-U.S. holder generally will be subject to U.S. federal income tax on any gain from the disposition of such stock if such Non-U.S. holder has owned or is deemed to have owned more than 5% of our Common Stock, at any time within the shorter of the five-year period preceding the disposition or such holder’s holding period for such stock.

If a Non-U.S. holder is subject to U.S. federal income tax on any sale, exchange, redemption (except as discussed below), or other disposition of the Common Stock, the Non-U.S. holder will recognize capital gain or loss equal to the difference between the amount realized by the Non-U.S. holder and the Non-U.S. holder’s adjusted tax basis in the Common Stock. Such capital gain or loss will be long-term capital gain or loss if the Non-U.S. holder’s holding period for the Common Stock is longer than one year. A Non-U.S. holder should consult its own independent tax advisors with respect to applicable tax rates and netting rules for capital gains and losses. Certain limitations exist on the deduction of capital losses by both corporate and non-corporate taxpayers.

If a Non-U.S. holder is subject to U.S. federal income tax on any disposition of the Common Stock, a redemption of shares of the Common Stock will be a taxable event. If the redemption is treated as a sale or exchange, instead of as a dividend, a Non-U.S. holder generally will recognize capital gain or loss, equal to the difference between the amount of cash received and fair market value of any property received and the Non-U.S. holder’s adjusted tax basis in the Common Stock redeemed (except that to the extent that any cash received is attributable to any accrued but unpaid dividends), and such capital gain or loss will be long-term capital gain or loss if the Non-U.S. holder’s holding period for such Common Stock exceeds one year. A payment made in redemption of the Common Stock may be treated as a dividend (subject to taxation as discussed above under “—*Disposition of Common Stock, Including Redemptions*”), rather than as payment in exchange for the Common Stock, in the same circumstances discussed above under “—*Disposition of Common Stock, Including Redemptions*.” Each Non-U.S. holder of the Common Stock should consult its own independent tax advisors to determine whether a payment made in redemption of the Common Stock will be treated as a dividend or as payment in exchange for the Common Stock.

Information reporting and backup withholding.

We must annually report to the IRS and to each Non-U.S. holder the amount of dividends (including constructive dividends) paid to such Non-U.S. holder and the tax withheld with respect to such dividends, regardless of whether withholding was required. Copies of the information returns reporting such dividends and withholding may also be made available under the provisions of an applicable tax treaty or agreement with the tax authorities in the country in which the non-U.S. holder resides. U.S. backup withholding will generally apply to the payment of dividends to non-U.S. holders unless such non-U.S. holders furnish to the payor an IRS Form W-8BEN or Form W-8BEN-E (or other applicable form) or otherwise establish an exemption.

Payment by a U.S. office of a broker of the proceeds of a sale of shares of our Common Stock is subject to both backup withholding and information reporting unless the non-U.S. holder, or beneficial owner thereof, as applicable, certifies that it is a non-U.S. holder on Form W-8BEN or Form W-8BEN-E (or other suitable substitute or successor form), or otherwise establishes an exemption. Subject to certain exceptions, backup withholding and information reporting generally will not apply to a payment of proceeds from the sale of shares of our Common Stock if such sale is effected through a foreign office of a broker, provided that the broker does not have certain U.S. connections. Any amount withheld under the backup withholding rules from a payment to a non-U.S. holder is allowable as a credit against such holder’s U.S. federal income tax liability (if any), which may entitle the holder to a refund if in excess of such liability, provided that the holder timely provides the required information to the IRS. Non-U.S. holders are

urged to consult their own tax advisers regarding the application of backup withholding in their particular circumstances and the availability of and procedure for obtaining an exemption from backup withholding under current Treasury Regulations.

Foreign Account Tax Compliance Act.

Sections 1471 to 1474 of the Code (such sections, and the Treasury Regulations and administrative guidance issued thereunder, commonly referred to as FATCA) impose a 30% U.S. withholding tax on certain “withholdable payments” made to a “foreign financial institution” or a “nonfinancial foreign entity.” “Withholdable payments” include payments of dividends and the gross proceeds from a disposition of certain property (such as shares of our Common Stock), if such disposition occurs after December 31, 2018. In general, if a holder is a “foreign financial institution” (which includes investment entities such as hedge funds and private equity funds), the 30% withholding tax will apply to withholdable payments made to such holder, unless such holder enters into an agreement with the U.S. Department of Treasury to collect and provide substantial information regarding its U.S. account holders, including certain account holders that are foreign entities with U.S. owners, and to withhold 30% on certain “pass-through payments.” If such holder is a “non-financial foreign entity,” FATCA also generally will impose a withholding tax of 30% on withholdable payments made to such holder unless the holder provides the withholding agent with a certification that it does not have any “substantial United States owners” or a certification identifying its direct and indirect substantial United States owners. Intergovernmental agreements between the United States and a holder’s resident country may modify some of the foregoing requirements.

Although withholding under FATCA would also have applied to payments of gross proceeds from the sale or other disposition of the Common Stock on or after January 1, 2019, Treasury Regulations proposed in late 2018 eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

We will not pay any additional amounts to holders of the Common Stock in respect of any amounts withheld. Non-U.S. holders should consult their own tax advisers with respect to the U.S. federal income tax consequences of FATCA on their ownership and disposition of shares of our Common Stock.

Documentation that holders provide in order to be treated as FATCA compliant may be reported to the IRS and other tax authorities, including information about a holder’s identity, its FATCA status and if applicable, its direct and indirect U.S. owners. Prospective investors should consult their tax advisers about how information reporting and the possible imposition of withholding tax under FATCA may apply to their investment in the Common Stock.

PLAN OF DISTRIBUTION

The Selling Stockholders, which as used herein includes certain donees, pledgees, transferees or other successors-in-interest selling Warrant Shares or interests in Warrant Shares received after the date of this prospectus from the Selling Stockholders as a gift, pledge, partnership distribution or other transfer, may, from time to time, sell, transfer or otherwise dispose of any or all of their Shares or interests in Warrant Shares on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These dispositions may be at fixed prices, at prevailing market prices at the time of sale, at prices related to the prevailing market price, at varying prices determined at the time of sale, or at negotiated prices.

The Selling Stockholders may use any one or more of the following methods when disposing of shares or interests therein:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- short sales effected after the date the registration statement of which this prospectus is a part is declared effective by the SEC;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- broker-dealers may agree with the Selling Stockholders to sell a specified number of such shares at a stipulated price per share;
- a combination of any such methods of sale; and
- any other method permitted by applicable law.

The Selling Stockholders may transfer the Warrant Shares in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

In connection with the sale of our Common Stock or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the Common Stock in the course of hedging the positions they assume. The Selling Stockholders may also sell shares of our Common Stock short and deliver these securities to close out its short positions, or loan or pledge the Common Stock to broker-dealers that in turn may sell these securities. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The aggregate proceeds to the Selling Stockholders from the sale of the Warrant Shares offered by them will be the sale price of the Warrant Shares less discounts or commissions, if any. The Selling Stockholders reserve the right to accept and, together with its agents from time to time, to reject, in whole or in part, any proposed purchase of Warrant Shares to be made directly or through agents. We will not receive any of the proceeds from this offering.

The Selling Stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act of 1933, provided that it meets the criteria and conform to the requirements of that rule.

The Selling Stockholders and any underwriters, broker-dealers or agents that participate in the sale of the Common Stock or interests therein may be “underwriters” within the meaning of Section 2(11) of the Securities Act. Any discounts, commissions, concessions or profit they earn on any resale of the shares may be underwriting discounts and commissions under the Securities Act. If any of the Selling Stockholders is an “underwriter” within the meaning of Section 2(11) of the Securities Act, it will be subject to the prospectus delivery requirements of the Securities Act.

To the extent required, the shares of our Common Stock to be sold, the names of the Selling Stockholders, the respective purchase prices and public offering prices, the names of any agents, dealer or underwriter, any applicable commissions or discounts with respect to a particular offer will be set forth in an accompanying prospectus supplement or, if appropriate, a post-effective amendment to the registration statement that includes this prospectus.

In order to comply with the securities laws of some states, if applicable, the Warrant Shares may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the Warrant Shares may not be sold unless it has been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have advised the Selling Stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the Selling Stockholders and their affiliates. In addition, to the extent applicable we will make copies of this prospectus (as it may be supplemented or amended from time to time) available to the Selling Stockholders for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The Selling Stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

We have agreed to indemnify the Selling Stockholders against liabilities, including liabilities under the Securities Act and the Exchange Act, relating to the registration of the shares offered by this prospectus.

We have agreed with the Selling Stockholders to keep the registration statement of which this prospectus constitutes a part effective at all times until no Selling Stockholder owns any Warrants or Warrant Shares.

Our Common Stock is listed on the Nasdaq Capital Market under the symbol “ATXI.”

LEGAL MATTERS

McGuireWoods LLP, Charlotte, North Carolina, will pass upon the validity of the securities being offered by this prospectus. 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 consolidated financial statements of Avenue Therapeutics, Inc. as of December 31, 2022 and for the year ended December 31, 2022 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 auditing and accounting. The audit report covering the December 31, 2022 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.

The financial statements of Avenue Therapeutics, Inc. as of December 31, 2021 and for the year ended December 31, 2021 incorporated by reference in this prospectus and in the registration statement have been so incorporated in reliance on the report of BDO USA, LLP (n/k/a BDO USA, P.C.), 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.

The financial statements of Baergic Bio, Inc. as of December 31, 2021 and 2020 and for each of the years in the two-year period ended December 31, 2021, 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 auditing and accounting. The audit report covering the December 31, 2021 financial statements contains an emphasis of matter paragraph that states that the Company’s recurring losses from operations raise substantial doubt about the entity’s ability to continue as a going concern. The 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.

We have filed with the SEC a registration statement on Form S-3 under the Securities Act relating to the securities being offered by this prospectus. This prospectus, which constitutes part of that registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules which are part of the registration statement. For further information about us and the securities offered, see the registration statement and the exhibits and schedules thereto. Statements contained in this prospectus regarding the contents of any contract or any other document to which reference is made are not necessarily complete, and, in each instance where a copy of a contract or other document has been filed as an exhibit to the registration statement, reference is made to the copy so filed, each of those statements being qualified in all respects by the reference.

INCORPORATION OF CERTAIN DOCUMENTS 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:

- (a) [our Annual Report on Form 10-K for the year ended December 31, 2022 \(the “2022 Form 10-K”\), filed with the SEC on March 31, 2023;](#)
- (b) our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2023, filed with the SEC on [May 12, 2023](#), the quarter ended June 30, 2023, filed with the SEC on [August 11, 2023](#), and the quarter ended September 30, 2023, filed with the SEC on [November 13, 2023](#);
- (c) [the information specifically incorporated by reference into the 2022 Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 28, 2023;](#)
- (d) our Current Reports on Form 8-K and Form 8-K/A filed with the SEC on [January 12, 2024](#), [January 8, 2024](#), [November 24, 2023](#), [November 2, 2023](#), [September 28, 2023](#), [September 27, 2023](#), [September 8, 2023](#), [July 21, 2023](#), [July 5, 2023](#), [June 26, 2023](#), [May 22, 2023](#), [April 17, 2023](#), [March 8, 2023](#), [March 2, 2023](#), [February 10, 2023](#), [February 3, 2023](#), [February 1, 2023](#) and [January 25, 2023](#); and
- (e) [the description of our Common Stock included in our registration statements on Form 8-A12B, filed with the SEC on June 14, 2017, and any amendment or report filed for the purpose of further updating such descriptions.](#)

We will furnish without charge to any person (including any beneficial owner) a copy of any or all of the documents incorporated by reference, including exhibits to these documents, upon written or oral request. Direct your 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.



Avenue Therapeutics, Inc.

33,080,598 Shares of Common Stock

PROSPECTUS

, 2024

PART II INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the SEC registration fee and the FINRA filing fee.

	Amount
SEC registration fee	\$ 679
Accounting fees and expenses	\$ 70,000
Legal fees and expenses	\$ 20,000
Miscellaneous fees and expenses	\$ —
Total expenses	\$ 90,679

Item 15. Indemnification of Directors and Officers

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

Section 145 of the DGCL grants to corporations the power to indemnify each officer and director against liabilities and expenses incurred by reason of the fact that he or she is or was an officer or director of the corporation if he or she acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The Company’s Third

Amended and Restated Certificate of Incorporation, as amended, and Second Amended and Restated Bylaws, as amended, provide for indemnification of each officer and director of the Company to the fullest extent permitted by the DGCL. Section 145 of the DGCL also empowers corporations to purchase and maintain insurance on behalf of any person who is or was an officer or director of the corporation against liability asserted against or incurred by him in any such capacity, whether or not the corporation would have the power to indemnify such officer or director against such liability under the provisions of Section 145 of the DGCL.

Item 16. Exhibits and Financial Statement Schedules

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

EXHIBIT INDEX

Exhibit No.	Description	Incorporated by Reference			Exhibit No.	Filed herewith
		Form	File Number	Date		
3.1	Form of Amendment to Third Amended and Restated Certificate of Incorporation					X
4.1	Specimen certificate evidencing shares of Common Stock	10-12G	000-55556	January 12, 2017	4.1	
4.2	Description of Securities of Avenue Therapeutics, Inc.	10-K	001-38114	March 31, 2023	4.3	
5.1	Opinion of McGuireWoods LLP					X
23.1	Consent of Independent Registered Public Accounting Firm, KPMG LLP as to Avenue Therapeutics, Inc., for year ended December 31, 2022					X
23.2	Consent of Independent Registered Public Accounting Firm, BDO USA, P.C as to Avenue Therapeutics, Inc.					X
23.3	Consent of Independent Registered Public Accounting Firm, KPMG LLP, as to Baergic Bio, Inc.					X
23.4	Consent of McGuireWoods LLP (included in Exhibit 5.1)					X
24.1	Power of Attorney (included in signature page hereto)					X
107	Filing Fee Table					X

Item 17. Undertakings

(a) The undersigned registrant hereby undertakes:

- (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:
 - (i) To include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;
 - (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement;
 - (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, however, that paragraphs (i), (ii) and (iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or, is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

- (3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.
- (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

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

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

- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:
- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
 - (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
 - (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
 - (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefits plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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- (c) Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act of 1933, as amended, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Securities Act of 1933, as amended, and will be governed by the final adjudication of such issue.
- (d) The undersigned registrant hereby undertakes that:
- (1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
 - (2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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SIGNATURES

Pursuant to the requirements of the Securities Act, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in Bay Harbor Islands, Florida, on January 24, 2024.

Avenue Therapeutics, Inc.

By: /s/ Alexandra MacLean
 Name: Alexandra MacLean, M.D.
 Title: Chief Executive Officer and Director

POWER OF ATTORNEY

Each person whose signature appears below constitutes and appoints each of Alexandra MacLean, M.D., and David Jin, acting alone or together with another attorney-in-fact, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for such person and in his or her name, place and stead, in any and all capacities, to sign any or all further amendments (including post-effective amendments) to this registration statement (and any additional registration statement related hereto permitted by Rule 462(b) promulgated under the Securities Act, (and all further amendments, including post-effective amendments, thereto)), and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dated indicated.

Signature	Title	Date
<u>/s/ Alexandra MacLean</u> Alexandra MacLean, M.D.	Chief Executive Officer and Director (Principal Executive Officer)	January 24, 2024
<u>/s/ David Jin</u> David Jin	Chief Operating Officer and Interim Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	January 24, 2024
<u>/s/ Jay Kranzler</u>	Chairman of the Board	January 24, 2024

Jay Kranzler, M.D., Ph.D.

/s/ Faith Charles
Faith Charles

Director

January 24, 2024

/s Neil Herskowitz
Neil Herskowitz

Director

January 24, 2024

/s/ Curtis Oltmans
Curtis Oltmans

Director

January 24, 2024

/s/ Lindsay A. Rosenwald
Lindsay A. Rosenwald, M.D.

Director

January 24, 2024

CERTIFICATE OF AMENDMENT

TO

THE THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

OF

AVENUE THERAPEUTICS, INC.

Avenue Therapeutics, Inc. (the "*Corporation*"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "*DGCL*"), does hereby certify:

FIRST. The Certificate of Incorporation of the Corporation is hereby amended by changing ARTICLE IV, so that, as amended, the first paragraph of said ARTICLE IV shall be amended and restated as follows:

Authorized Stock. The total number of shares of all classes of capital stock that the Corporation shall have the authority to issue is (i) two hundred million (200,000,000) shares of Common Stock, with \$0.0001 par value, and (ii) two million (2,000,000) shares of Preferred Stock, with \$.0001 par value (the "*Preferred Stock*"), 250,000 of which are designated as Class A Preferred Stock (the "*Class A Preferred Stock*") and the remainder are undesignated Preferred Stock.

SECOND. That a resolution was duly adopted by unanimous written consent of the directors of the Corporation, pursuant to Section 242 of the DGCL, setting forth the above mentioned amendment to the Certificate of Incorporation and declaring said amendment to be advisable.

THIRD. That this amendment was duly adopted by the holders of a majority of the voting power of the Corporation by written consent, pursuant to Section 228 of the DGCL.

IN WITNESS WHEREOF, this Certificate of Amendment of the Certificate of Incorporation has been signed by the Chief Executive Officer of the Corporation this ____ day of _____, 2024.

AVENUE THERAPEUTICS, INC.

By: _____

Name: Alexandra MacLean, M.D.

Title: Chief Executive Officer



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January 24, 2024

Avenue Therapeutics, Inc.
 1111 Kane Concourse, Suite 301
 Bay Harbor Islands, FL 33154

RE: Registration Statement on Form S-3

Ladies and Gentlemen:

We have acted as counsel to Avenue Therapeutics, Inc., a Delaware corporation (the “Company”), in connection with the Registration Statement on Form S-3 (the “Registration Statement”) being filed by the Company on the date of this opinion letter with the Securities and Exchange Commission (the “SEC”) under the Securities Act of 1933, as amended (the “Securities Act”). The Registration Statement relates to the registration of the offer and resale by certain selling stockholders of the Company of up to 33,080,598 shares of the Company’s Common Stock, par value \$0.0001 per share (“Common Stock”), consisting of (i) 16,540,299 shares of the Company’s Common Stock issuable upon exercise of the Company’s outstanding Series A Warrants to purchase Common Stock previously issued to the selling stockholders (the “Series A Warrant Shares”) and (ii) 16,540,299 shares of Common Stock issuable upon the exercise of the Company’s outstanding Series B Warrants to purchase Common Stock previously issued to the selling stockholders (the “Series B Warrant Shares” and, together with the Series A Warrant Shares, the “Securities”).

This opinion letter is being furnished in accordance with the requirements of Item 16 of Form S-3 and Item 601(b)(5)(i) of Regulation S-K promulgated under the Securities Act. The Securities are described in the Registration Statement. Capitalized terms used and not defined herein shall have the meanings assigned to them in the Registration Statement.

Documents Reviewed

In connection with this opinion letter, we have examined:

- (a) the Registration Statement, including the exhibits being filed therewith and incorporated by reference therein from previous filings made by the Company with the SEC;
- (b) the prospectus contained in the Registration Statement (the “Prospectus”); and
- (c) the Series A Warrants to purchase Common Stock (the “Series A Warrants”); and
- (d) the Series B Warrants to purchase Common Stock (the “Series B Warrants”); and
- (e) the form of Certificate of Amendment to the Company’s Third Amended and Restated Certificate of Incorporation to be filed with the Secretary of State of the State of Delaware, substantially in the form filed as Exhibit 3.1 to the Registration Statement (the “Certificate of Amendment”) and, together with the Series A Warrant and the Series B Warrant, the “Subject Documents”).

Avenue Therapeutics, Inc.
 January 24, 2024
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In addition, we have examined and relied upon the following:

- (i) a certificate from the Corporate Secretary of the Company certifying as to (A) true and correct copies of the Third Amended and Restated Certificate of Incorporation of the Company and Second Amended and Restated Bylaws of the Company, each as in effect the date hereof and as amended to date, and (B) the resolutions of the Board of Directors of the Company authorizing (1) the filing of the Registration Statement by the Company; and (2) the Securities issued and issuable by the Company;
- (ii) a certificate dated January 24, 2024 issued by the Secretary of State of the State of Delaware, attesting to the corporate status of the Company in the State of Delaware; and
- (iii) originals, or copies identified to our satisfaction as being true copies, of such other records, documents and instruments as we have deemed necessary for the purposes of this opinion letter.

“Applicable Law” means the Delaware General Corporation Law.

Assumptions Underlying Our Opinions

For all purposes of the opinions expressed herein, we have assumed, without independent investigation, the following:

- (a) **Factual Matters**. To the extent that we have reviewed and relied upon (i) certificates of the Company or authorized representatives thereof, (ii) representations of the Company set forth in the Subject Documents (if any) and (iii) certificates and assurances from public officials, all of such certificates, representations and assurances are accurate with regard to factual matters and all official records (including filings with public authorities) are properly indexed and filed and are accurate and complete.
- (b) **Signatures**. The signatures of individuals who signed the Subject Documents are genuine and (other than those of individuals signing on behalf of the Company at or before the date hereof) authorized.

(c) Authentic and Conforming Documents. All documents submitted to us as originals are authentic, complete and accurate, and all documents submitted to us as copies conform to authentic original documents.

(d) Subject Documents. All parties to the Subject Documents have the requisite power and authority (corporate or otherwise) to enter into and perform all obligations under such agreements or instruments, that the Subject Documents have been duly authorized by all requisite action (corporate or otherwise) and executed and delivered by such parties and that such agreements or instruments are the valid, binding and enforceable obligations of such parties, except that no such assumptions are made with respect to the Company.

(e) Registration. The Registration Statement shall have been declared effective under the Securities Act, and such effectiveness shall not have been terminated or rescinded.

Our Opinions

Based on and subject to the foregoing and the exclusions, qualifications, limitations and other assumptions set forth in this opinion letter, we are of the opinion that upon the effectiveness of the Certificate of Amendment, the Securities have been duly authorized and, when issued and delivered in accordance with the terms of the Subject Documents, will be validly issued, fully paid and non-assessable.

Avenue Therapeutics, Inc.
January 24, 2024
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Our opinions set forth above are limited to the Applicable Law, and we do not express any opinion concerning any other law.

Miscellaneous

The foregoing opinions are being furnished only for the purpose referred to in the first paragraph of this opinion letter. Our opinions are based on statutes, regulations and administrative and judicial interpretations which are subject to change. We undertake no responsibility to update or supplement these opinions subsequent to the effective date of the Registration Statement. Headings in this opinion letter are intended for convenience of reference only and shall not affect its interpretation. We hereby consent to the filing of this opinion as Exhibit 5.1 to the Registration Statement on or about the date hereof, to the incorporation by reference of this opinion of counsel into the Registration Statement and to the reference to our firm in the Prospectus under the caption "Legal Matters." In giving this consent, we do not admit that we are within the category of persons whose consent is required by Section 7 of the Securities Act or the rules and regulations of the SEC promulgated thereunder.

Very truly yours,

/s/ McGuireWoods LLP

McGuireWoods LLP

Consent of Independent Registered Public Accounting Firm

We consent to the use of our report dated March 31, 2023, with respect to the consolidated financial statements of Avenue Therapeutics, Inc., incorporated herein by reference, and to the reference to our firm under the heading “Experts” in the prospectus.

/s/ KPMG LLP

New York, New York
January 24, 2024

Consent of Independent Registered Public Accounting Firm

Avenue Therapeutics, Inc.
Bay Harbor Islands, FL

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement of our report dated March 25, 2022, relating to the financial statements of Avenue Therapeutics, Inc. appearing in the Company's Annual Report on Form 10-K for the year ended December 31, 2022. Our report contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

We also consent to the reference to us under the caption "Experts" in the Prospectus.

/s/ BDO USA, P.C.

New York, NY
January 24, 2024

Consent of Independent Registered Public Accounting Firm

We consent to the use of our report dated August 31, 2022, with respect to the financial statements of Baergic Bio, Inc., incorporated herein by reference, and to the reference to our firm under the heading “Experts” in the prospectus.

/s/ KPMG LLP

New York, New York
January 24, 2024

Calculation of Filing Fee Tables

Form S-3

(Form Type)

Avenue Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

Security Type	Security Class Title	Fee Calculation Rule ⁽¹⁾	Amount Registered ⁽²⁾	Proposed Maximum Offering Price Per Unit ⁽¹⁾	Maximum Aggregate Offering Price ⁽¹⁾	Fee Rate	Amount of Registration Fee
Equity	Common Stock, par value \$0.0001 per share	457(c)	33,080,598 ⁽³⁾	\$ 0.139 ⁽²⁾	\$ 4,598,203.12	0.00014760	\$ 678.69
Total Offering Amounts					<u>\$ 4,598,203.12</u>		<u>\$ 678.69</u>
Total Fee Offsets							<u>—</u>
Net Fee Due							<u>\$ 678.69</u>

(1) Pursuant to Rule 457(c) under the Securities Act, and solely for the purpose of calculating the registration fee, the proposed maximum offering price per share is the average of the high and low prices reported for the registrant's Common Stock quoted on The Nasdaq Capital Market LLC on January 23, 2024.

(2) Pursuant to Rule 416(a) under the Securities Act, this registration statement also covers an indeterminate number of additional shares as may be issuable as a result of stock splits, stock dividends or similar transactions.

(3) Represents 33,080,598 shares of Common Stock issuable upon the exercise of common stock purchase warrants to purchase one share of Common Stock at an exercise price of \$0.3006, issued to certain selling stockholders on January 9, 2024.