

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, DC 20549

FORM S-8

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)

**1111 Kane Concourse, Suite 301**  
**Bay Harbor Islands, Florida 33154**  
(Address of Principal Executive Offices)

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

**33154**  
(Zip Code)

**Avenue Therapeutics, Inc. 2015 Incentive Plan, as Amended**  
(Full title of the plan)

**Alexandra MacLean, M.D.**  
*Chief Executive Officer*  
**1111 Kane Concourse, Suite 301**  
**Bay Harbor Islands, Florida 33154**  
**(781) 652-4500**

(Name, address, and telephone number of agent for service)

Copy to:

**Rakesh Gopalan**  
**David S. Wolpa**  
**Troutman Pepper Hamilton Sanders LLP**  
**301 S. College Street, 34<sup>th</sup> Floor**  
**Charlotte, North Carolina 28202**  
**(704) 998-4050**

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b2 of the Exchange Act. (Check one):

Large accelerated filer   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
Emerging growth company

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.

**INCORPORATION BY REFERENCE OF CONTENTS  
OF REGISTRATION STATEMENT ON FORM S-8**

This Registration Statement is being filed by Avenue Therapeutics, Inc. (the "Registrant") for the purpose of registering the offer and sale of an additional 5,000,000 shares of common stock, \$0.0001 par value per share (the "Common Stock"), that are issuable pursuant to the Registrant's 2015 Incentive Plan, as amended (the "Plan"). These additional shares of Common Stock are securities of the same class as other securities for which a Registration Statement on Form S-8 of the Registrant relating to the same stock incentive plan is effective. The Registrant previously registered the offer and sale of shares of Common Stock issuable under the Plan under a Registration Statement on Form S-8 filed with the Securities and Exchange Commission (the "Commission") on [August 15, 2017 \(File No. 333-219972\)](#), as amended by a Registration Statement on Form S-8, filed with the Commission on [December 17, 2021 \(File No. 333-261710\)](#), and a Registration Statement on Form S-8 filed with the Commission on [February 10, 2023 \(File No. 333-269689\)](#). Pursuant to General Instruction E to Form S-8, this Registration Statement hereby incorporates by reference the contents of the Registration Statements referenced above.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

## Item 8. Exhibits

The Exhibits listed on the Exhibit Index of this Registration Statement are filed herewith or are incorporated by reference to other filings.

### EXHIBIT INDEX

Exhibit Number	Description
<a href="#">4.1</a>	<a href="#">Third Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38114) filed with the Commission on June 27, 2017).</a>
<a href="#">4.2</a>	<a href="#">Certificate of Amendment of the Third Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38114) filed with the Commission on August 14, 2018).</a>
<a href="#">4.3</a>	<a href="#">Certificate of Amendment of the Third Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38114) filed with the Commission on February 3, 2023).</a>
<a href="#">4.4</a>	<a href="#">Certificate of Amendment of the Third Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38114) filed with the Commission on February 23, 2024).</a>
<a href="#">4.5</a>	<a href="#">Certificate of Amendment of the Third Amended and Restated Certificate of Incorporation of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38114) filed with the Commission on April 26, 2024).</a>
<a href="#">4.6</a>	<a href="#">Second Amended and Restated Bylaws of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-38114) filed with the Commission on February 10, 2023).</a>
<a href="#">5.1*</a>	<a href="#">Opinion of Troutman Pepper Hamilton Sanders LLP</a>
<a href="#">23.1*</a>	<a href="#">Consent of KPMG LLP</a>
<a href="#">23.2*</a>	<a href="#">Consent of Troutman Pepper Hamilton Sanders LLP (included in Exhibit 5.1 to this Registration Statement on Form S-8)</a>
<a href="#">24.1*</a>	<a href="#">Powers of Attorney (included on signature pages to this registration statement)</a>
<a href="#">99.1</a>	<a href="#">Avenue Therapeutics, Inc. 2015 Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Form 10-12G (File No. 000-55556) filed with the Commission on January 12, 2017).</a>
<a href="#">99.2</a>	<a href="#">Amendment to the Avenue Therapeutics, Inc. 2015 Incentive Plan (incorporated by reference to Exhibit 99.2 to the Registrant's Form S-8 (File No. 333-261710) filed with the Commission on December 17, 2021).</a>
<a href="#">99.3</a>	<a href="#">Amendment to the Avenue Therapeutics, Inc. 2015 Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (file No. 001-38114) filed with the Commission on February 3, 2023).</a>
<a href="#">99.4</a>	<a href="#">Amendment to the Avenue Therapeutics, Inc. 2015 Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (file No. 001-38114) filed with the Commission on June 26, 2024).</a>
<a href="#">107.*</a>	<a href="#">Filing Fee Table</a>

\*Filed herewith

### SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Bay Harbor Islands, State of Florida, on this 12<sup>th</sup> day of July, 2024.

#### Avenue Therapeutics, Inc.

By: /s/ Alexandra MacLean, M.D.

Name: Alexandra MacLean, M.D.  
Title: Chief Executive Officer

### POWERS OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below hereby constitutes and appoints each of Alexandra MacLean, M.D. and David Jin, as his or her true and lawful attorney-in-fact and agent, with power to act without any other and with full and several power of substitution, for him or her and in his or her name, place and stead, to sign, in his or her capacity or capacities as shown below, any and all amendments to this Registration Statement on Form S-8 (including post-effective amendments), and to file the same, with all exhibits thereto, and all 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 connection with any such amendments, as fully for all intents and purposes as he or she might or could do in person, and does hereby ratify and confirm all that said attorneys-in-fact and agents, or either of them, or their substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed below by the following persons in the capacities and on the dates indicated.

Signature	Date	Title
<u>/s/ Alexandra MacLean, M.D.</u> Alexandra MacLean, M.D.	July 12, 2024	Chief Executive Officer (Principle Executive Officer)
<u>/s/ David Jin</u> David Jin	July 12, 2024	Interim Chief Financial Officer and Chief Operating Officer (Principal Financial and Accounting Officer)
<u>/s/ Lindsay A. Rosenwald, M.D.</u> Lindsay A. Rosenwald, M.D.	July 12, 2024	Executive Chairman of the Board
<u>/s/ Faith Charles</u> Faith Charles	July 12, 2024	Director
<u>/s/ Neil Herskowitz</u> Neil Herskowitz	July 12, 2024	Director
<u>/s/ Jay Kranzler, M.D., PhD</u>	July 12, 2024	Director

Jay Kranzler, M.D., PhD

/s/ Curtis Oltmans  
Curtis Oltmans

July 12, 2024

Director

[Letterhead of Troutman Pepper Hamilton Sanders LLP]

July 12, 2024

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

Re: Registration Statement on Form S-8: 5,000,000 Shares of Common Stock issuable under the Avenue Therapeutics, Inc. 2015 Incentive Plan

Ladies and Gentlemen:

We have acted as counsel to Avenue Therapeutics, Inc., a Delaware corporation (the "Company"), in connection with the Company's registration statement on Form S-8 (the "Registration Statement"), filed on the date hereof, with the U.S. Securities and Exchange Commission (the "Commission"), under the Securities Act of 1933, as amended (the "Securities Act"). The Registration Statement relates to the registration of the offer, sale and issuance of 5,000,000 shares (the "Shares") of the Company's common stock, par value \$0.0001 per share (the "Common Stock"), from time to time pursuant to the Avenue Therapeutics, Inc. 2015 Incentive Plan, as amended (the "Plan").

This opinion letter is being furnished in accordance with the requirements of Item 8 of Form S-8 and Item 601(b)(5)(i) of Regulation S-K promulgated under the Securities Act. Capitalized terms used and not defined herein shall have the meanings assigned to them in the Registration Statement.

In connection with this opinion, we have reviewed the corporate proceedings taken by the Company with respect to the offer and sale of the Shares under the Plan, and the registration thereof under the Securities Act. We have also examined and relied upon originals or copies of such corporate records, documents, agreements or other instruments of the Company, and such certificates and records of public officials, and such other documents, as we have deemed necessary or appropriate in connection herewith, including, but not limited to, the Company's Third Amended and Restated Certificate of Incorporation, as amended, the Company's Second Amended and Restated Bylaws and the Plan pursuant to which the Shares are issuable. As to all matters of fact (including, without limitation, factual conclusions and characterizations and descriptions of purpose, intention or other state of mind) we have relied entirely upon a certificate of an officer of the Company, and have assumed, without independent inquiry, the accuracy of that certificate.

In rendering this opinion, we have assumed the genuineness and authenticity of all signatures on the original documents; the legal capacity of all natural persons; the authenticity of all documents submitted to us as originals; the conformity to originals of all documents submitted to us as certified or photocopies; the accuracy and completeness of all documents and records reviewed by us; the accuracy, completeness and authenticity of certificates issued by any governmental official, office or agency and the absence of change in the information contained therein from the effective date of any such certificate; and the due authorization, execution and delivery of all documents where authorization, execution and delivery are prerequisites to the effectiveness of such documents, except that we make no such assumption with respect to the Company.

Our opinion is expressed only with respect to the General Corporation Law of the State of Delaware. We are not opining as to the applicability thereto, or the effect thereon, of the laws of any other jurisdiction or, in the case of Delaware, any other laws, or as to matters of municipal law or the laws of any local agencies within any states (including "blue sky" or other state securities laws).

Based upon the foregoing, we are of the opinion that, as of the date hereof, the Shares have been duly authorized, and, when issued and paid for in accordance with the terms and upon the terms and conditions of the Plan, will be validly issued, fully paid and non-assessable.

We assume no obligation to supplement this opinion if any applicable law changes after the date hereof or if we become aware of any fact that might change the opinion expressed herein after the date hereof.

We hereby consent to the filing of this opinion as Exhibit 5.1 to the Registration Statement. In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission. Except as otherwise set forth herein, this opinion may not be used, circulated, quoted or otherwise referred to for any purpose or relied upon by any other person without the express written permission of this firm.

Very truly yours,

/s/ Troutman Pepper Hamilton Sanders LLP  
Troutman Pepper Hamilton Sanders LLP

**Consent of Independent Registered Public Accounting Firm**

We consent to the use of our report dated March 18, 2024, with respect to the consolidated financial statements of Avenue Therapeutics, Inc., incorporated herein by reference.

/s/ KPMG LLP

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New York, NY  
July 12, 2024

## Calculation of Filing Fee Tables

**Form S-8**

(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	Other	5,000,000	\$ 3.335(2)	\$ 16,675,000	0.00014760	\$ 2,461.23
<b>Total Offering Amounts</b>						\$ 16,675,000	\$ 2,461.23
<b>Total Fee Offsets</b>							—
<b>Net Fee Due</b>							\$ 2,461.23

(1) Pursuant to Rules 457(c) and 457(h) 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 July 5, 2024.

(2) Represents 5,000,000 additional shares reserved for issuance under the Avenue Therapeutics, Inc. 2015 Incentive Plan, as amended (the "Plan"). Pursuant to Rule 416(a) under the Securities Act, this registration statement also covers an indeterminate number of additional shares as may be necessary to account for adjustment provisions under the Plan as a result of stock splits, stock dividends or similar transactions.