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**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, DC 20549

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**FORM S-8**

**REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933**

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**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, Florida 33154**  
(Address of Principal Executive Offices)

**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**

(Name and address of agent for service)

**(781) 652-4500**

(Telephone number, including area code, of agent for service)

Copy to:

**Rakesh Gopalan**

**David S. Wolpa**

**McGuireWoods LLP**

**201 N. Tryon St., Suite 3000**

**Charlotte, NC 28202**

**(704) 343-2000**

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.

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**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 \(File No. 333-261710\)](#). Pursuant to General Instruction E to Form S-8, this Registration Statement hereby incorporates by reference the contents of the Registration Statements referenced above.

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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 herein 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 of 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 of 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 of 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="#">Amended and Restated Bylaws of Avenue Therapeutics, Inc. (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-38114) filed with the Commission on February 11, 2019).</a>
<a href="#">5.1*</a>	<a href="#">Opinion of McGuireWoods LLP regarding legality of the securities being registered hereby</a>
<a href="#">23.1*</a>	<a href="#">Consent of Independent Registered Public Accounting Firm, BDO USA, LLP</a>
<a href="#">23.2*</a>	<a href="#">Consent of McGuireWoods 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 page)</a>
<a href="#">99.1</a>	<a href="#">Avenue Therapeutics, Inc. 2015 Incentive Plan (incorporated by reference to Exhibit 10.7 of 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 of 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 of the Registrant's Current Report on Form 8-K (file No. 001-38114) filed with the Commission on February 3, 2023).</a>
<a href="#">107.*</a>	<a href="#">Filing Fee Table</a>

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 10th day of February, 2023.

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.	February 10, 2023	Chief Executive Officer (Principal Executive Officer)
<u>/s/ David Jin</u> David Jin	February 10, 2023	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.	February 10, 2023	Executive Chairman of the Board
<u>/s/ Faith Charles</u> Faith Charles	February 10, 2023	Director
<u>/s/ Neil Herskowitz</u> Neil Herskowitz	February 10, 2023	Director
<u>/s/ Jay Kranzler, M.D., PhD</u> Jay Kranzler, M.D., PhD	February 10, 2023	Director

/s/ Curtis Oltmans  
Curtis Oltmans

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February 10, 2023

Director

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# McGUIREWOODS

201 North Tryon Street  
Suite 3000  
Charlotte, North Carolina 28202

February 10, 2023

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

RE: Registration Statement on Form S-8

5,000,000 Shares of Common Stock of Avenue Therapeutics, Inc. to be issued pursuant to 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") that is being filed on the date hereof with the Securities and Exchange Commission ("SEC"), pursuant to the Securities Act of 1933, as amended (the "Securities Act"), relating to the registration of the 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"). For purposes of clarification, the Shares exclude shares of the Company's Common Stock previously authorized under 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.

In connection with this opinion letter, we have examined the Registration Statement, including the exhibits being filed therewith or incorporated by reference therein. In addition, we have examined and relied upon the following:

- (i) a certificate from an officer of the Company certifying as to (A) true and correct copies of the Third Amended and Restated Certificate of Incorporation of the Company and Amended and Restated Bylaws of the Company, each as in effect the date hereof and as amended to date, (B) the resolutions of the Board of Directors of the Company with respect to the Shares and the Registration Statement, and (C) the proposal adopted by the stockholders of the Company relating to the amendment to the Plan at the Company's 2022 Annual Meeting of Stockholders;
- (ii) a certificate dated February 9, 2023 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.

**McGuireWoods LLP | [www.mcguirewoods.com](http://www.mcguirewoods.com)**

Atlanta | Austin | Baltimore | Charlotte | Charlottesville | Chicago | Dallas | Houston | Jacksonville | London | Los Angeles - Century City  
Los Angeles - Downtown | New York | Norfolk | Pittsburgh | Raleigh | Richmond | San Francisco | Tysons | Washington, D.C.

Avenue Therapeutics, Inc.  
February 10, 2023  
Page 2

For all purposes of the opinions expressed herein, we have assumed, without independent investigation, the following: (a) to the extent that we have reviewed and relied upon certificates of the Company or authorized representatives thereof and certificates and assurances from public officials, all of such certificates and assurances are accurate with regard to factual matters; (b) 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; (c) the genuineness of all signatures; and (d) the Registration Statement will be effective under the Securities Act.

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 the Shares have been duly authorized, and, when issued in accordance with the terms and upon the terms and conditions of the Plan upon receipt of the Company of adequate consideration for the Shares specified therein, will be validly issued, fully paid and non-assessable.

The foregoing opinion is limited to the Delaware General Corporation Law (including statutory provisions, all applicable provisions of the Delaware Constitution and reported judicial decisions interpreting the foregoing), as in effect on the date hereof, and we do not express any opinion concerning any other law.

The foregoing opinion is being furnished only for the purpose referred to in the first paragraph of this opinion letter. We hereby consent to the filing of this opinion as Exhibit 5.1 to the Registration Statement. 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

Avenue Therapeutics, Inc.  
Bay Harbor Islands, FL

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 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, 2021. Our report contains an explanatory paragraph regarding the Company's ability to continue as a going concern.

/s/ BDO USA, LLP

New York, New York

February 10, 2023

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## 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 <sup>(1)</sup>	Amount Registered <sup>(2)</sup>	Proposed Maximum Offering Price Per Unit <sup>(1)</sup>	Maximum Aggregate Offering Price <sup>(1)</sup>	Fee Rate	Amount of Registration Fee
Fees to Be Paid	Equity	Common Stock, \$0.0001 par value per share	Other	5,000,000	\$1.24	\$6,200,000.00	\$ 0.00011020	\$683.24
	<b>Total Offering Amounts</b>					6,200,000.00		\$683.24
	<b>Total Fees Previously Paid</b>							\$0
	<b>Total Fee Offsets</b>							\$0
		<b>Net Fee Due</b>						\$683.24

- (1) Pursuant to Rules 457(c) and 457(h) under the Securities Act of 1933, as amended (the "Securities Act"), and solely for the purpose of calculating the registration fee, the proposed maximum offering share price is the average of the high and low prices for the Registrant's Common Stock reported by The Nasdaq Capital Market on February 9, 2023.
- (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 shall also cover an indeterminate number of shares as may be necessary to account for adjustment provisions under the Plan as a result of stock dividend, stock split, recapitalization or other similar transaction.