Registration No. 333-

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

FORM S-8

REGISTRATION STATEMENT

Under

The Securities Act of 1933

AXSOME THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

45-4241907

(IRS Employer Identification No.)

22 Cortlandt Street 16th Floor New York, New York 10007 (Address of principal executive offices) (Zip Code)

Axsome Therapeutics, Inc. Amended and Restated 2015 Omnibus Incentive Compensation Plan (Full title of the Plans)

> Herriot Tabuteau, M.D. President and Chief Executive Officer Axsome Therapeutics, Inc. 22 Cortlandt Street 16th Floor New York, New York 10007 (Name and address of agent for service) (212) 332-3241 (Telephone number, including area code, of agent for service)

> > Copies to:

Emilo Ragosa DLA Piper LLP (US) 51 John F. Kennedy Parkway, Suite 120 Short Hills, New Jersey 07078 Telephone: (973) 520-2550

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. (Check one):

Large accelerated filer \boxtimes Non-accelerated filer \square Accelerated filer \Box Smaller reporting company \Box

Emerging growth company \Box

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.

PART II

Information Required in the Registration Statement

This Registration Statement relates to the registration of an additional 1,512,671 shares (the "Shares") of the common stock, par value \$0.0001 per share, of Axsome Therapeutics, Inc. (the "Registrant"). The Shares are securities of the same class and relate to the same employee benefit plan, the 2015 Omnibus Incentive Compensation Plan, as those registered pursuant to the Registrant's registration statements on Form S-8, previously filed with the Securities and Exchange Commission on December 16, 2015, March 29, 2017, August 13, 2018, March 15, 2019, May 11, 2020 and May 11, 2021. In accordance with General Instruction E of Form S-8, the contents of the Registrant's registration statements on Form S-8 (File Nos. 333-208579, 333-217002, 333-226824, 333-230296, 333-238174 and 333-256019) filed with the Securities and Exchange Commission on December 16, 2017, August 13, 2018, March 15, 2019, May 11, 2020 and May 11, 2021 are incorporated herein by reference and the information required by Part II is omitted, except as supplemented by the information set forth below.

Item 8. Exhibits

Exhibit Number	Exhibit
5.1*	<u>Opinion and Consent of DLA Piper LLP (US).</u>
23.1*	Consent of DLA Piper LLP (US) is contained in Exhibit 5.1.
23.2*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
24.1*	Power of Attorney. Reference is made to page 4 of this Registration Statement.
99.1	Axsome Therapeutics, Inc. Amended and Restated 2015 Omnibus Incentive Compensation Plan (Incorporated by reference, Exhibit 10.2 to Registrant's Quarterly Report on Form 10-Q, filed on August 10, 2020).
99.2	Axsome Therapeutics, Inc. Form of Stock Option Agreement pursuant to the Amended and Restated 2015 Omnibus Incentive Compensation Plan (Incorporated by reference, Exhibit 99.2 to Registrant's Registration Statement on Form S-8, File No. 333-208579, filed December 16, 2015).
99.3	Axsome Therapeutics, Inc. Form of Restricted Stock Unit Agreement (Non-Executives) pursuant to the Amended and Restated 2015 Omnibus Incentive Compensation Plan (Incorporated by reference, Exhibit 99.3 to the Company's Registration Statement on Form S-8 (File No. 333-238174), filed May 11, 2020).
99.4	Axsome Therapeutics, Inc. Form of Restricted Stock Unit Agreement (Executives and Non-Employee Directors) pursuant to the Amended and Restated 2015 Omnibus Incentive Compensation Plan (Incorporated by reference, Exhibit 99.4 to the Company's Registration Statement on Form S-8 (File No. 333-238174), filed May 11, 2020).
107*	Filing Fee Table.
* Filed herewit	h

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, 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 New York, State of New York on this 2nd day of May, 2022.

AXSOME THERAPEUTICS, INC.

By /s/ Herriot Tabuteau, M.D.

Herriot Tabuteau, M.D. *Chief Executive Officer*

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS:

That each person whose signature appears below constitutes and appoints Herriot Tabuteau, M.D., Chief Executive Officer, and Nick Pizzie, Chief Financial Officer, and each of them, as such person's true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for such person and in such person's name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, 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 connection therewith, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitutes, may lawfully do or cause to be done by virtue thereof.

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

Signature	Title	Date
/s/ Herriot Tabuteau, M.D.	Chief Executive Officer and Chairman of the Board (Principal Executive Officer)	May 2, 2022
Herriot Tabuteau, M.D.		
/s/ Nick Pizzie, CPA, MBA	Chief Financial Officer	May 2, 2022
Nick Pizzie, CPA, MBA	(Principal Financial and Accounting Officer)	
/s/ Mark Coleman, M.D.	Director	May 2, 2022
Mark Coleman, M.D.		
/s/ Roger Jeffs, Ph.D.	Director	May 2, 2022
Roger Jeffs, Ph.D.		
/s/ Mark Saad	Director	May 2, 2022
Mark Saad		

Exhibit 5.1 DLA Piper LLP (US) 51 John F. Kennedy Parkway, Suite 120 Short Hills, New Jersey 07078 www.dlapiper.com T: 973-520-2550 F: 973-520-2551 Attorney Responsible for Short Hills Office: Emilio Ragosa

May 2, 2022

Axsome Therapeutics, Inc. 22 Cortlandt Street, 16th Floor New York, New York 10007

Re: Axsome Therapeutics, Inc. - Registration Statement on Form S-8

Dear Ladies and Gentlemen:

We have acted as counsel to Axsome Therapeutics, Inc., a Delaware corporation (the "Company"), in connection with the preparation of a Registration Statement on Form S-8 (the "Registration Statement") under the Securities Act of 1933, as amended (the "Act"). The Registration Statement relates to the registration of 1,512,671 shares (the "Plan Shares") of the Company's common stock, par value \$0.0001 per share (the "Common Stock"), issuable under the Axsome Therapeutics, Inc. Amended and Restated 2015 Omnibus Incentive Compensation Plan (the "Plan"), as referenced in the Registration Statement.

In connection with this opinion letter, we have examined the Registration Statement and originals, or copies certified or otherwise identified to our satisfaction, of the Amended and Restated Certificate of Incorporation and the Amended and Restated Bylaws of the Company and such other documents, records and other instruments as we have deemed appropriate for purposes of the opinion set forth herein.

We have assumed the genuineness of all signatures, the legal capacity of all natural persons, the authenticity of the documents submitted to us as originals, the conformity with the originals of all documents submitted to us as certified, facsimile or photostatic copies and the authenticity of the originals of all documents submitted to us as certified.

Based upon the foregoing, we are of the opinion that the Plan Shares have been duly authorized and, when and to the extent issued in accordance with the terms of the Plan and any award agreement entered into under the Plan, the Plan Shares will be validly issued, fully paid and nonassessable.

The opinion expressed herein is limited to the Delaware General Corporation Law.

We hereby consent to the use of this opinion as Exhibit 5.1 to the Registration Statement. In giving such consent, we do not hereby admit that we are acting within the category of persons whose consent is required under Section 7 of the Act or the rules or regulations of the U.S. Securities and Exchange Commission thereunder.

Very truly yours,

/s/ DLA Piper LLP (US)

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the Axsome Therapeutics, Inc. 2015 Omnibus Incentive Compensation Plan of our reports dated March 1, 2022, with respect to the consolidated financial statements of Axsome Therapeutics, Inc. and the effectiveness of internal control over financial reporting of Axsome Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2021, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP New York, NY May 2, 2022

Calculation Of Filing Fee Tables Form S-8 (Form Type) Axsome Therapeutics, Inc. (Exact Name of Registrant as Specified in its Charter) Table 1: Newly Registered Securities

				Proposed				
				Maximum				
		Fee		Offering	Maximum		A	mount of
Security	Security Class	Calculation	Amount	Price Per	Aggregate		Re	gistration
Type	Title	Rule	Registered(1)	Unit	Offering Price	Fee Rate		Fee
	Common stock,							
	\$0.0001 par value per	Rule 457(c) and						
Equity	share	Rule 457(h)	1,512,671(2)	\$ 31.15(3)	\$47,119,701.65	\$ 0.0000927	\$	4,368.00
	Total Offering A			\$47,119,701.65		\$	4,368.00	
Total Fee Offsets								-
Net Fee Due							\$	4,368.00

- (1) Pursuant to Rule 416(a) under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement (the "Registration Statement") shall also cover any additional shares of the Registrant's common stock, \$0.0001 par value per share (the "Common Stock") that becomes issuable under the Registrant's Amended and Restated 2015 Omnibus Incentive Compensation Plan (the "Plan") by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without the receipt of consideration that increases the number of the Registrant's outstanding shares of Common Stock.
- (2) This Registration Statement covers 1,512,671 shares of the Registrant's Common Stock, which are issuable pursuant to the Plan.
- (3) Estimated in accordance with Rule 457(c) and (h) under the Securities Act solely for the purpose of calculating the registration fee on the basis of \$31.15, the average of the high and low prices of the Registrant's common stock as reported on The Nasdaq Global Market on April 28, 2022.