As filed with the Securities and Exchange Commission on August 7, 2025

Registration No. 333-

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	**45-4241907**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

One World Trade Center
29th Floor
New York, New York 10007
(Address of principal executive offices) (Zip Code)

Axsome Therapeutics, Inc. 2025 Long-Term Incentive Plan
(Full title of the Plans)

Herriot Tabuteau, M.D.
President and Chief Executive Officer
Axsome Therapeutics, Inc.
One World Trade Center
29th 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:

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

Hunter Murdock
General Counsel
Axsome Therapeutics, Inc.
One World Trade Center
29th Floor
New York, NY 10007
Telephone: (212) 332-3241

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 ☒	Accelerated filer ☐
Non-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. ☐

PART I

INFORMATION REQUIRED IN THE SECTION 10(a) PROSPECTUS

Item 1. Plan Information

The information required by Item 1 is included in documents sent or given to participants in the plans covered by this Registration Statement pursuant to Rule 428(b)(1) of the Securities Act of 1933, as amended (the "1933 Act").

Item 2. Registrant Information and Employee Plan Annual Information

The written statement required by Item 2 is included in documents sent or given to participants in the plans covered by this Registration Statement pursuant to Rule 428(b)(1) of the 1933 Act.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference

The following documents filed by the Registrant with the Commission pursuant to the Securities Exchange Act of 1934, as amended (the "Exchange Act"), are hereby incorporated by reference herein and shall be deemed to be a part hereof:

(a) The Registrant's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the Commission on February 18, 2025;

(b) All other reports filed pursuant to Section 13(a) or 15(d) of the 1934 Act since the end of the fiscal year covered by the Registrant's Annual Report on Form 10-K for the year ended December 31, 2024 referred to in (a) above; and

(c) The Registrant's Registration Statement on Form 8-A filed with the Commission on November 16, 2015 pursuant to Section 12(b) of the 1934 Act, in which there is described the terms, rights, and provisions applicable to the Registrant's outstanding Common Stock.

All reports and definitive proxy or information statements filed pursuant to Section 13(a), 13(c), 14 or 15(d) of the 1934 Act after the date of this Registration Statement and prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which de-registers all securities then remaining unsold shall be deemed to be incorporated by reference into this Registration Statement and to be a part hereof from the date of filing of such documents. Unless expressly incorporated into this Registration Statement, a report furnished but not filed on Form 8-K under the 1934 Act shall not be incorporated by reference into this Registration Statement. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained herein or in any subsequently filed document which also is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.

Item 4. Description of Securities

Not Applicable.

Item 5. Interests of Named Experts and Counsel

Not Applicable.

Item 6. Indemnification of Directors and Officers

As permitted by the Delaware General Corporation Law, the Registrant has adopted provisions in its amended and restated certificate of incorporation and amended and restated by-laws that limit or eliminate the personal liability of its directors. Consequently, a director will not be personally liable to the Registrant or the Registrant's stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for: (i) any breach of the director's duty of loyalty to the Registrant or the Registrant's stockholders; (ii) any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law; (iii) any unlawful payments related to dividends or unlawful stock repurchases, redemptions or other distributions; or (iv) any transaction from which the director derived an improper personal benefit.

These limitations of liability do not alter director liability under the federal securities laws and do not affect the availability of equitable remedies such as an injunction or rescission.

In addition, the Registrant's amended and restated by-laws provide that: (i) the Registrant will indemnify its directors, officers and, in the discretion of its board of directors, certain employees to the fullest extent permitted by the Delaware General Corporation Law; and (ii) advance expenses, including attorneys' fees, to the Registrant's directors and, in the discretion of the Registrant's board of directors, to its officers and certain employees, in connection with legal proceedings, subject to limited exceptions.

The Registrant's amended and restated certificate of incorporation that became effective immediately prior to the completion of its initial public offering provides that the Registrant will indemnify each of its directors to the fullest extent permitted by the Delaware General Corporation Law and advance expenses to each indemnitee in connection with any proceeding in which indemnification is available.

The Registrant also maintains general liability insurance to provide insurance coverage to its directors and officers for losses arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the 1933 Act. Insofar as indemnification for liabilities arising under the 1933 Act may be permitted to directors, officers, or persons controlling the Registrant pursuant to the foregoing provisions, the Registrant has been informed that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

These provisions may discourage stockholders from bringing a lawsuit against the Registrant's directors in the future for any breach of their fiduciary duty. These provisions may also have the effect of reducing the likelihood of derivative litigation against directors and officers, even though such an action, if successful, might otherwise benefit the Registrant and its stockholders. Furthermore, a stockholder's investment may be adversely affected to the extent the Registrant pays the costs of settlement and damage awards against directors, officers and certain employees pursuant to these indemnification provisions. The Registrant believes that these provisions, the indemnification agreements and the insurance are necessary to attract and retain talented and experienced directors and officers.

Item 7. Exemption from Registration Claimed

Not Applicable.

Item 8. Exhibits

Exhibit Number	Exhibit
4.1	Amended and Restated Certificate of Incorporation of the Company (Incorporated by reference, Exhibit 3.1 to the Company's Current Report on Form 8-K (No. 001-37635) filed November 24, 2015).
4.2	Amended and Restated Bylaws of the Company (Incorporated by reference, Exhibit 3.2 to the Company's Current Report on Form 8-K (No. 001-37635 filed November 24, 2015).
4.3	Specimen Certificate evidencing shares of Company's common stock (Incorporated by reference, Exhibit 4.1 to Amendment No. 1 to the Company's Registration Statement on Form S-1 (No. 333-207393) filed October 30, 2015).
4.4	Description of Securities (Incorporated by reference, Exhibit 4.13 to the Company's Annual Report on Form 10-K filed March 12, 2020).
5.1*	Opinion and Consent of DLA Piper LLP (US).
23.1*	Consent of DLA Piper LLP (US) is contained in Exhibit 5.1.
23.2*	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm.
23.3*	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.
24.1*	Power of Attorney. Reference is made to page 6 of this Registration Statement.
99.1	Axsome Therapeutics, Inc. 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed August 4, 2025).
99.2	Axsome Therapeutics, Inc. Form of Standard Restricted Stock Units Agreement pursuant to the 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed August 4, 2025).
99.3	Axsome Therapeutics, Inc. Form of Director Restricted Stock Units Agreement pursuant to the 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2025).
99.4	Axsome Therapeutics, Inc. Form of Executive Deferral Restricted Stock Units Agreement pursuant to the 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2025).
99.5	Axsome Therapeutics, Inc. Form of Standard Nonstatutory Stock Option Agreement pursuant to the 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2025).
99.6	Axsome Therapeutics, Inc. Form of Director Nonstatutory Stock Option Agreement pursuant to the 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2025).
99.7	Axsome Therapeutics, Inc. Form of Performance-Based Restricted Stock Unit Agreement pursuant to the 2025 Long-Term Incentive Plan (Incorporated by reference, Exhibit 10.10 to the Company's Quarterly Report on Form 10-Q filed on August 4, 2025).
107*	Filing Fee Table.

* Filed herewith

Item 9. 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 this 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 this Registration Statement;

(iii) To include any material information with respect to the plan of distribution not previously disclosed in this Registration Statement or any material change to such information in this Registration Statement; provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the Commission by Registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this 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.

(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 Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in this 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.

(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 Act 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 whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

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 7th day of August, 2025.

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. Herriot Tabuteau, M.D.	Chief Executive Officer and Chairman of the Board (Principal Executive Officer)	August 7, 2025
/s/ Nick Pizzie, CPA, M.B.A. Nick Pizzie, CPA, M.B.A.	Chief Financial Officer (Principal Financial and Accounting Officer)	August 7, 2025
/s/ Mark Coleman, M.D. Mark Coleman, M.D.	Director	August 7, 2025
/s/ Roger Jeffs, Ph.D. Roger Jeffs, Ph.D.	Director	August 7, 2025
/s/ Susan Mahony, Ph.D., M.B.A. Susan Mahony, Ph.D., M.B.A.	Director	August 7, 2025
/s/ Mark Saad Mark Saad	Director	August 7, 2025

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

August 7, 2025

Axsome Therapeutics, Inc.
One World Trade Center, 29th 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 3,000,000 shares of common stock (the "Plan Shares") of the Company's common stock, par value $0.0001 per share, issuable under the Axsome Therapeutics, Inc. 2025 Long-Term Incentive 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 copies.

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)

DLA Piper LLP (US)

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in this Registration Statement on Form S-8 of our reports dated February 18, 2025 relating to the financial statements of Axsome Therapeutics, Inc. and the effectiveness of Axsome Therapeutics, Inc.'s internal control over financial reporting, appearing in the Annual Report on Form 10-K of Axsome Therapeutics, Inc. for the year ended December 31, 2024.

/s/ Deloitte & Touche LLP

Morristown, New Jersey

August 7, 2025

Exhibit 23.3

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. 2025 Long-Term Incentive Plan of our report dated February 27, 2023, with respect to the consolidated financial statements of Axsome Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2024, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

New York, NY
August 7, 2025

EXHIBIT 107

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

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered[1][2]	Proposed Maximum Offering Price Per Unit[3]	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Equity	Common stock, $0.0001 par value per share	Rule 457(c) and Rule 457(h)	3,000,000	$ 102.73	$ 308,190,000	$ 0.00015310	$ 47,184
	Total Offering Amounts				$ 308,190,000		$ 47,184
	Total Fee Offsets						—
	Net Fee Due						$ 47,184

(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 ("Common Stock") that become issuable pursuant to the Registrant's 2025 Long-Term Incentive Plan (the "2025 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) Such number includes 2,500,000 shares of the Registrant's Common Stock under the 2025 Plan and an additional 500,000 shares of the Registrant's Common Stock under the Amended and Restated 2015 Omnibus Incentive Compensation Plan that may be forfeited and rolled over into the 2025 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 $102.73, the average of the high and low prices of the Registrant's Common Stock as reported on The Nasdaq Global Market on August 6, 2025.