Registration No. 333-

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

FORM S-8 REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

SAGE THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization) 27-4486580 (I.R.S. Employer Identification No.)

215 First Street Cambridge, MA 02142 (Address of Principal Executive Offices)

Sage Therapeutics, Inc. 2014 Stock Option and Incentive Plan (Full Title of the Plans)

> Barry E. Greene President and Chief Executive Officer Sage Therapeutics, Inc. 215 First Street Cambridge, MA 02142 (617) 299-8380 (Name and Address of Agent For Service)

> > Copy to:

Anne Marie Cook Senior Vice President, General Counsel Sage Therapeutics, Inc. 215 First Street Cambridge, MA 02142 (617) 299-8380 Stuart M. Falber, Esq. Rosemary G. Reilly, Esq. Wilmer Cutler Pickering Hale and Dorr LLP 60 State Street Boston, MA 02109 (617) 526-6000

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 \square

Non-accelerated filer

accelerated files employ reporting company.

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. \Box

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price per Share(2)	Proposed Maximum Aggregate Offering Price(2)	Amount of Registration Fee
Common Stock, \$0.0001 par value per share	2,332,336 shares (3)	\$79.86	\$186,260,352.96	\$20,321.01

- Pursuant to Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement shall also cover any additional shares of common stock, \$0.0001 par value per share ("Common Stock"), which become issuable under the Registrant's 2014 Stock Option and Incentive Plan (the "Plan") by reason of any stock dividend, stock split, recapitalization or any other similar transaction effected without the receipt of consideration which results in an increase in the number of the Registrant's outstanding shares of Common Stock.
 (2) Estimated called for the number of an entire the number of the Registrant's outstanding shares of common Stock.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) of the Securities Act, and based on the average of the high and low sale prices of the Registrant's Common Stock, as quoted on the Nasdaq Global Market, on February 18, 2021.
- (3) Represents an automatic increase to the number of shares available for issuance under the Plan, effective January 1, 2021. Shares available for issuance under the Plan were previously registered on registration statements on Form S-8 filed with the Securities and Exchange Commission on July 18, 2014 (Registration No. 333-197498), May 29, 2015 (Registration No. 333-204549), February 29, 2016 (Registration No. 333-209831), February 23, 2017 (Registration No. 333-216202), February 22, 2018 (Registration No. 333-223146), February 19, 2019 (Registration No. 333-229732), and February 27, 2020 (Registration No. 333-236680).

EXPLANATORY NOTE

This Registration Statement on Form S-8 registers additional shares of Common Stock under the Plan. The number of shares of Common Stock reserved and available for issuance under the Plan is subject to an automatic annual increase on each January 1 by an amount equal to four percent of the number of shares of Common Stock issued and outstanding on the immediately preceding December 31 or such lesser number of shares of Common Stock as determined by the Administrator (as defined in the Plan). Accordingly, on January 1, 2021, the number of shares of Common Stock reserved and available for issuance under the Plan increased by 2,332,336. This Registration Statement registers these additional 2,332,336 shares of Common Stock. The additional shares are of the same class as other securities relating to the Plan for which a registration statement on Form S-8 has previously been filed and is effective. The information contained in the following registration statements filed on Form S-8 by the Registrant is hereby incorporated by reference pursuant to General Instruction E, except in each case with respect to "Item 8. Exhibits" thereof:

- 1) Registration Statement on Form S-8 (Registration No. 333-197498) filed on July 18, 2014;
- 2) Registration Statement on Form S-8 (Registration No. 333-204549) filed on May 29, 2015;
- 3) Registration Statement on Form S-8 (Registration No. 333-209831) filed on February 29, 2016;
- 4) Registration Statement on <u>Form S-8</u> (Registration No. 333-216202) filed on February 23, 2017;
- 5) Registration Statement on Form S-8 (Registration No. 333-223146) filed on February 22, 2018;
- 6) Registration Statement on <u>Form S-8</u> (Registration No. 333-229732) filed on February 19, 2019; and
- 7) Registration Statement on Form S-8 (Registration No. 333-236680) filed on February 27, 2020.

Part II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 8. Exhibits.

Exhibit <u>No.</u>	Description			
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1, as amended (File No. 333-196849) filed on July 8, 2014)			
4.2	Fifth Amended and Restated Certificate of Incorporation of the Registrant, as currently in effect (incorporated by reference to Exhibit 3.1 of the Registrant's Current Report on Form 8-K (File No. 001-36544) filed on July 25, 2014)			
4.3	Amended and Restated Bylaws of the Registrant, as amended on August 6, 2020 (incorporated by reference to Exhibit 3.1 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 10, 2020)			
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP			
23.1*	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm			
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)			
24.1*	Power of Attorney (included on the signature pages of this registration statement)			
99.1	2014 Stock Option and Incentive Plan and forms of agreements thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's			

99.2 <u>Registration Statement on Form S-1, as amended (File No. 333-196849) filed on July 8, 2014)</u>
 99.2 <u>Form of Performance-Based Restricted Stock Unit Award Agreement Under the Sage Therapeutics, Inc. 2014 Stock Option and Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-36544) filed on August 10, 2020)</u>

* Filed herewith.

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 Cambridge, Commonwealth of Massachusetts, on the 24th day of February, 2021.

SAGE THERAPEUTICS, INC.

By: /s/ Barry E. Greene

Barry E. Greene Chief Executive Officer, President and Director

POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Sage Therapeutics, Inc., hereby severally constitute and appoint Barry E. Greene and Kimi Iguchi, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him or her and in his or her name, place and stead, and in any and all capacities, to sign for us and in our names in the capacities indicated below any and all amendments (including post-effective amendments) to this Registration Statement on Form S-8, 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 or necessary to be done in and about the premises, as full to all intents and purposes as he or she 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 substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Barry E. Greene Barry E. Greene	Chief Executive Officer, President and Director (Principal Executive Officer)	February 24, 2021
/s/ Kimi Iguchi Kimi Iguchi	Chief Financial Officer (Principal Financial and Accounting Officer)	February 24, 2021
/s/ Michael F. Cola Michael F. Cola	Director	February 24, 2021
/s/ Steven Paul Steven Paul, M.D.	Director	February 24, 2021
/s/ Kevin P. Starr Kevin P. Starr	Director	February 24, 2021

/s/ James Frates James Frates	_ Director	February 24, 2021
/s/ Geno Germano Geno Germano	_ Director	February 24, 2021
/s/ Jeffrey M. Jonas Jeffrey M. Jonas, M.D.	_ Director	February 24, 2021
/s/ Elizabeth Barrett Elizabeth Barrett	_ Director	February 24, 2021
/s/ George Golumbeski George Golumbeski, Ph.D.	_ Director	February 24, 2021

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Exhibit 5.1

+1 617 526 6000 (t) +1 617 526 5000 (f) wilmerhale.com

February 24, 2021

Sage Therapeutics, Inc. 215 First Street Cambridge, MA 02142

Re: 2014 Stock Option and Incentive Plan

Ladies and Gentlemen:

We have assisted in the preparation of a Registration Statement on Form S-8 (the "<u>Registration Statement</u>") to be filed with the Securities and Exchange Commission (the "<u>Commission</u>") under the Securities Act of 1933, as amended (the "<u>Securities Act</u>"), relating to an aggregate of 2,332,336 shares of common stock, \$0.0001 par value per share (the "<u>Shares</u>"), of Sage Therapeutics, Inc., a Delaware corporation (the "<u>Company</u>"), issuable under the Company's 2014 Stock Option and Incentive Plan (the "<u>Plan</u>").

We have examined the Certificate of Incorporation and Bylaws of the Company, each as amended and restated to date, and originals, or copies certified to our satisfaction, of all pertinent records of the meetings of the directors and stockholders of the Company, the Registration Statement and such other documents relating to the Company as we have deemed material for the purposes of this opinion.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified, photostatic or other copies, the authenticity of the originals of any such documents and the legal competence of all signatories to such documents.

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares in accordance with the Plan to register and qualify the Shares for sale under all applicable state securities or "blue sky" laws.

We express no opinion herein as to the laws of any state or jurisdiction other than the state laws of the Commonwealth of Massachusetts, the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters.

Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109 Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto San Francisco Washington

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Sage Therapeutics Inc. February 24, 2021 Page 2

Based on the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and, when the Shares are issued and paid for in accordance with the terms and conditions of the Plan, the Shares will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion with the Commission in connection with the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act. 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.

Very truly yours,

WILMER CUTLER PICKERING HALE AND DORR LLP

By: /s/ Rosemary G. Reilly Rosemary G. Reilly, a Partner

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 of Sage Therapeutics, Inc. of our report dated February 24, 2021, relating to the financial statements, and the effectiveness of internal control over financial reporting, which appears in Sage Therapeutics, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2020.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts February 24, 2021