Registration No. 333-

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-8

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

Lexicon Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization) 76-0474169 (I.R.S. Employer Identification No.)

77381

(Zip Code)

2445 Technology Forest Blvd., 11th Floor The Woodlands, Texas (Address of Principal Executive Offices)

> 2017 Non-Employee Directors' Equity Incentive Plan (Full titles of the plan)

> > Lonnel Coats President and Chief Executive Officer 2445 Technology Forest Blvd., 11th Floor The Woodlands, Texas 77381

(281) 863-3000

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

copies to:

David P. Oelman Vinson & Elkins L.L.P. 1001 Fannin, Suite 2500 Houston, Texas 77002-6760 (713) 758-2222 Brian T. Crum Vice President and General Counsel Lexicon Pharmaceuticals, Inc. 2445 Technology Forest Blvd., 11th Floor The Woodlands, Texas 77381 (281) 863-3000

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," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. Large accelerated filer 0 Accelerated filer \square Non-accelerated filer 0 Smaller reporting company \square Emerging growth company 0

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 13(a) of the Exchange Act. 0

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Title of Plan	Amount to be Registered (1)	Proposed Maximum Offering Price Per Share (2)	Proposed Maximum Aggregate Offering Price (2)	Amount of Registration Fee
Common Stock, par value \$0.001	2017 Non-Employee Directors' Equity Incentive Plan	600,000 shares \$	3.55 \$	2,130,000 \$	233

(1) Pursuant to Rule 416(a) under the Securities Act of 1933, this registration statement shall be deemed to cover any additional shares of common stock that become issuable under the 2017 Non-Employee Directors' Equity Incentive Plan to prevent dilution resulting from stock splits, stock dividends or similar transactions.

2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457 (c) and (h) under the Securities Act of 1933. The proposed maximum offering price per share, proposed maximum aggregate offering price and amount of registration fee are based on the average of the high and low sales price per share of the registration's common stock, as reported on The Nasdaq Global Select Market on August 2, 2021.

EXPLANATORY NOTE

Lexicon Pharmaceuticals, Inc. (the "Company") previously filed registration statements on Form S-8 (Registration Nos. 333-41532, 333-188020, 333-210145, 333-217873, 333-234569 and 333-240169) registering the issuance of an aggregate of 600,000 shares of the Company's common stock under its 2017 Non-Employee Directors' Equity Incentive Plan.

On April 29, 2021, the Company's stockholders approved an amendment of the 2017 Non-Employee Directors' Equity Incentive Plan that increased the total number of shares of the Company's common stock that may be issued pursuant to stock awards granted under the plan from 600,000 to 1,200,000 shares.

Pursuant to General Instruction E to Form S-8 under the Securities Act of 1933, as amended, this registration statement on Form S-8 is being filed by the Company for the purpose of registering the issuance of an additional 600,000 shares of the Company's common stock under the 2017 Non-Employee Directors' Equity Incentive Plan as a result of such increase in the number of shares reserved for issuance under the plan. This registration statement will increase the number of shares registered under the 2017 Non-Employee Directors' Equity Incentive Plan to 1,200,000 shares. The content contained in the Company's registration statements on Form S-8 (Registration Nos. 333-41532, 333-168678, 333-183020, 333-210145, 333-217873, 333-234569 and 333-240169) is hereby incorporated by reference pursuant to General Instruction E.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

<u>Exhibit No.</u>

Item 8. Exhibits.

Exhibit No.		Description
4.1	—	Second Amended and Restated Certificate of Incorporation (filed as Exhibit 3.1 to the Company's Current Report on Form 8-K dated April 29, 2021 and incorporated by reference herein).
4.2	—	<u>Second Amended and Restated Bylaws</u> (filed as Exhibit 3.2 to the Company's Current Report on Form 8-K dated April 26, 2012 and incorporated by reference herein).
4.3	—	Securities Purchase Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein).
4.4	—	<u>Amendment, dated October 7, 2009, to Securities Purchase Agreement</u> , dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated October 7, 2009 and incorporated by reference herein).
4.5	—	Registration Rights Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.3 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein).
4.6	_	Stockholders' Agreement, dated June 17, 2007, with Invus, L.P. (filed as Exhibit 10.4 to the Company's Current Report on Form 8-K dated June 17, 2007 and incorporated by reference herein).
4.7	—	<u>Supplement to Transaction Agreements</u> , dated March 15, 2010, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated March 15, 2010 and incorporated by reference herein).
4.8	_	Supplement No. 2 to Transaction Agreements, dated February 23, 2012, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated February 23, 2012 and incorporated by reference herein).
4.9	—	Supplement No. 3 to the Transaction Agreements, dated December 16, 2020, with Invus, L.P. and Invus C.V. (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated December 16, 2020 and incorporated by reference herein).
4.10	—	Indenture related to the 5.25% Convertible Senior Notes due 2021, dated as of November 26, 2014, with Wells Fargo Bank, N.A. (filed as Exhibit 4.1 to the Company's Current Report on Form 8-K dated November 26, 2014 and incorporated by reference herein).
4.11	—	Form of 5.25% Convertible Senior Notes due 2021 (filed as Exhibit 4.2 to the Company's Current Report on Form 8-K dated November 26, 2014 and incorporated by reference herein).
*4.12	_	Description of Common Stock.
*5.1	_	Opinion of Vinson & Elkins L.L.P.
*23.1	_	Consent of Independent Registered Public Accounting Firm
*23.2	_	Consent of Vinson & Elkins L.L.P. (contained in Exhibit 5.1).
*24.1	_	Power of Attorney (contained in signature page).
99.1	—	2017 Non-Employee Directors' Equity Incentive Plan (filed as Exhibit 10.1 to the Company's Current Report on Form 8-K dated April 29, 2021 and incorporated by reference herein).

* 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 The Woodlands, in the State of Texas, on August 6, 2021.

Lexicon Pharmaceuticals, Inc.

By: /s/ Lonnel Coats

Lonnel Coats
President and Chief Executive Officer

POWER OF ATTORNEY

Each person whose signature appears below appoints Lonnel Coats and Jeffrey L. Wade, and each of them, any of whom may act without the joinder of the other, as his or her true and lawful attorneys-in-fact and agents with full power of substitution and resubstitution, for him or her and in his or her 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 all other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite and necessary to be done, as fully to all intents and purposes as he might or would do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his substitute and 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 DATES INDICATED BELOW.

<u>Signature</u>	Title	Date
/s/ Lonnel Coats	President, Chief Executive Officer and Director (Principal Executive Officer)	August 6, 2021
Lonnel Coats	(Thicipal Executive Officer)	
/s/ Jeffrey L. Wade	Executive Vice President, Corporate and Administrative Affairs and Chief	August 6, 2021
Jeffrey L. Wade	Financial Officer (Principal Financial Officer)	
/s/ James F. Tessmer	Vice President, Finance and Accounting	August 6, 2021
James F. Tessmer	(Principal Accounting Officer)	
/s/ Raymond Debbane	Chairman of the Board of Directors	August 6, 2021
Raymond Debbane		
/s/ Philippe J. Amouyal	Director	August 6, 2021

Philippe J. Amouyal

/s/ Samuel L. Barker	Director	August 6, 2
Samuel L. Barker, Ph.D.	-	
/s/ Robert J. Lefkowitz	Director	August 6, 2
Robert J. Lefkowitz, M.D.		
/s/ Alan S. Nies	Director	August 6, 2
Alan S. Nies, M.D.		
/s/ Frank P. Palantoni	Director	August 6, 2
Frank P. Palantoni		
/s/ Christopher J. Sobecki	Director	August 6, 2
Christopher J. Sobecki	_	
/s/ Judith L. Swain	Director	August 6, 2
Judith L. Swain, M.D.	_	

DESCRIPTION OF COMMON STOCK

Authorized Common Stock

We are authorized to issue up to 225 million shares of common stock, par value \$0.001 per share.

The following summary description of our common stock is based on the provisions of our second amended and restated certificate of incorporation, second amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our second amended and restated certificate of incorporation, second amended and restated bylaws and the Delaware General Corporation Law. For more detailed information about the rights of our common stock, you should refer to our second amended and restated certificate of incorporation amended and restated certificate of incorporation amended and restated and restated bylaws and the Delaware General Corporation and second amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law.

Voting Rights

The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election.

Dividend Rights

Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably such dividends as may be declared by the board of directors out of funds legally available therefor.

Liquidation Rights

Upon the liquidation, dissolution or winding up of Lexicon, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any outstanding shares of preferred stock.

Preemptive and Consent Rights

Holders of 20% or more of our issued and outstanding common stock have (a) customary preemptive rights related to the issuance of certain of our securities and (b) consent rights prior us taking any of the following actions: (i) creating or issuing any new class or series of shares of capital stock (or securities convertible into or exercisable for shares of capital stock) having rights, preferences or privileges senior to or on parity with the common stock, (ii) subject to certain exceptions, repurchasing, retiring, redeeming or otherwise acquiring any of our equity securities (or securities convertible into or exchangeable for equity securities) or any subsidiary and (iii) adopting, or proposing to adopt, or maintaining any shareholders' rights plan, "poison pill" or other similar plan or agreement, unless such stockholder is exempt from such plan or agreement.

No Redemption or Sinking Fund Provisions

There are no redemption or sinking fund provisions applicable to our common stock.

Fully Paid and Non-assessable

All outstanding shares of our common stock are fully paid and non-assessable.

Arrangements with Invus

In June 2007, we entered into a securities purchase agreement with Invus, L.P., under which Invus, L.P. made an initial investment in our common stock in August 2007.

Board of Directors. Concurrently with the execution of the securities purchase agreement, we entered into a stockholders' agreement with Invus, L.P. under which Invus, L.P. and its affiliates (collectively, "Invus") have the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus, rounded up to the nearest whole number of directors. Invus has designated three of the nine current members of our board of directors. While Invus has not presently exercised its director designation rights in full, it may exercise them at any time in the future in its sole discretion. To facilitate the exercise of such rights, we have agreed, upon written request from Invus, to take all necessary actions in accordance with our obligations under the stockholders' agreement to (a) increase the number of directors to the number specified by Invus (which number shall be no greater than reasonably necessary for the exercise of Invus' director designation rights under the stockholders' agreement) and (b) cause the appointment to the newly created directorships of directors so designated by Invus pursuant to its rights under the stockholders' agreement.

Invus also has the right to require proportionate representation of Invus-appointed directors on the audit, compensation and corporate governance committees of our board of directors, subject to certain restrictions. Invus-designated directors currently serve as one of the three members of each of the compensation committee and the corporate governance committee of our board of directors. No Invus-designated directors currently serve on the audit committee of our board of directors.

The provisions of the stockholders' agreement relating to Invus' rights to designate members of our board of directors and its audit, compensation and corporate governance committees will terminate if the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%. Invus also has the right to terminate these provisions at any time in its discretion.

Registration Rights. Concurrently with the execution of the securities purchase agreement, we also entered into a registration rights agreement with Invus, L.P., pursuant to which Invus has certain demand and piggyback registration rights with respect to shares of our common stock held by them.

Preemptive and Consent Rights. Our second amended and restated certificate of incorporation grants holders of 20% or more of our issued and outstanding common stock (a) customary preemptive rights related to the issuance of certain of our securities and (b) consent rights prior us taking any of the following actions: (i) creating or issuing any new class or series of shares of capital stock (or securities convertible into or exercisable for shares of capital stock) having rights, preferences or privileges senior to or on parity with the common stock, (ii) subject to certain exceptions, repurchasing, retiring, redeeming or otherwise acquiring any of our equity securities (or securities convertible into or exchangeable for equity securities) or any subsidiary and (iii) adopting, or proposing to adopt, or maintaining any shareholders' rights plan, "poison pill" or other similar plan or agreement, unless such stockholder is exempt from such plan or agreement. Based on Invus' current ownership interest in our common stock, Invus possesses such preemptive and consent rights.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Delaware Takeover Statute. We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly-held Delaware corporation such as Lexicon from engaging in a business combination with an interested stockholder for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner. For purposes of Section 203, a business combination includes a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns (or within three years prior, did own) 15% or more of our voting stock.

Charter Documents. Our second amended and restated certificate of incorporation requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by a consent in writing. Additionally, our second amended and restated certificate of incorporation:

- does not provide for the use of cumulative voting in the election of directors;
- provides for a board of directors, classified into three classes of directors;
- provides that the authorized number of directors may be changed only by resolution of our board of directors; and
- provides for the authority of our board of directors to issue up to five million shares of "blank check" preferred stock and to determine the price, powers, preferences and rights of these shares, without stockholder approval.

Our second amended and restated bylaws provide that candidates for director may be nominated only by our board of directors or by a stockholder who gives written notice to us not less than 120 days nor more than 150 days in advance of the first anniversary of the date of our proxy statement relating to the previous year's annual meeting of stockholders. The authorized number of directors is fixed in accordance with our second amended and restated certificate of incorporation. Our board of directors currently consists of nine members, divided into three classes. As a result, a portion of the board of directors will be elected each year. The board of directors may appoint new directors to fill vacancies or newly created directorships. Our second amended and restated bylaws also limit who may call a special meeting of stockholders.

Delaware law and these charter provisions may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Inc.

August 6, 2021

Lexicon Pharmaceuticals, Inc. 2445 Technology Forest Blvd., 11th Floor The Woodlands, Texas 77381

Re: Registration Statement on Form S-8

Ladies and Gentlemen:

We have acted as counsel for Lexicon Pharmaceuticals, Inc., a Delaware corporation (the "Company"), in connection with the Company's registration under the Securities Act of 1933, as amended (the "Act"), of the offer and sale of an aggregate of up to 600,000 shares of the Company's common stock, par value \$0.001 per share (the "Shares"), pursuant to the Company's registration statement on Form S-8 (the "Registration Statement") to be filed with the Securities and Exchange Commission on August 6, 2021, which Shares may be issued from time to time in accordance with the terms of the Lexicon Pharmaceuticals, Inc. 2017 Non-Employee Directors' Equity Incentive Plan (as it may be amended from time to time, the "Plan").

In reaching the opinions set forth herein, we have examined and are familiar with originals or copies, certified or otherwise identified to our satisfaction, of such documents and records of the Company and such statutes, regulations and other instruments as we deemed necessary or advisable for purposes of this opinion, including (i) the Registration Statement, (ii) certain resolutions adopted by the board of directors of the Company, (iii) the Plan, and (iv) such other certificates, instruments, and documents as we have considered necessary for purposes of this opinion. As to any facts material to our opinions, we have made no independent investigation or verification of such facts and have relied, to the extent that we deem such reliance proper, upon certificates of public officials and officers or other representatives of the Company.

We have assumed (i) the legal capacity of all natural persons, (ii) the genuineness of all signatures, (iii) the authority of all persons signing all documents submitted to us on behalf of the parties to such documents, (iv) the authenticity of all documents submitted to us as originals, (v) the conformity to authentic original documents of all documents submitted to us as copies, (vi) that all information contained in all documents reviewed by us is true, correct and complete, and (vii) that the Shares will be issued in accordance with the terms of the Plan.

Based on the foregoing and subject to the limitations set forth herein, and having due regard for the legal considerations we deem relevant, we are of the opinion that the Shares have been duly authorized and, when the Shares are issued by the Company in accordance with the terms of the Plan and the instruments executed pursuant to the Plan, as applicable, that govern the awards to which any Share relates, the Shares will be validly issued, fully paid and non-assessable.

This opinion is limited in all respects to the General Corporation Law of the State of Delaware. We express no opinion as to any other law or any matter other than as expressly set forth above, and no opinion as to any other law or matter may be inferred or implied herefrom. The opinions expressed herein are rendered as of the date hereof and we expressly disclaim any obligation to update this letter or advise you of any change in any matter after the date hereof.

This opinion may be filed as an exhibit to the Registration Statement. In giving this consent, we do not thereby admit that we come within the category of persons whose consent is required under Section 7 of the Act.

Very truly yours,

/s/ Vinson & Elkins L.L.P.

Vinson & Elkins L.L.P.

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the 2017 Non-Employee Directors' Equity Incentive Plan of Lexicon Pharmaceuticals, Inc. of our reports dated March 12, 2021, with respect to the consolidated financial statements of Lexicon Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Lexicon Pharmaceuticals, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Houston, Texas August 6, 2021