

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC. 20549

SCHEDULE 14A
(Rule 14A-101)

INFORMATION REQUIRED IN PROXY STATEMENT
SCHEDULE 14A INFORMATION

Proxy Statement Pursuant to Section 14(a) of
the Securities Exchange Act of 1934

Filed by the Registrant
Filed by a Party other than the Registrant
Check the appropriate box:

- Preliminary Proxy Statement Confidential, for Use of the Commission Only
 Definitive Proxy Statement (as permitted by Rule 14a-6(e)(2))
 Definitive Additional Materials
 Soliciting Material Pursuant to Rule 14a-11(c) or Rule 14a-12

LEXICON PHARMACEUTICALS, INC.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if Other Than the Registrant)

Payment of Filing Fee (Check the appropriate box):

No fee required.

Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

- (1) Title of each class of securities to which transaction applies: N/A
(2) Aggregate number of securities to which transaction applies: N/A
(3) Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined): N/A
(4) Proposed maximum aggregate value of transaction: N/A

Fee paid previously with preliminary materials: N/A

Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

(5) Total fee paid: \$0

- (1) Amount Previously Paid:
(2) Form, Schedule or Registration Statement No.:
(3) Filing Party:
(4) Date Filed



April 8, 2022

TO OUR STOCKHOLDERS:

I am pleased to invite you to attend the 2022 annual meeting of stockholders of Lexicon Pharmaceuticals, Inc. to be held on Friday, May 20, 2022 at 8:00 a.m. CDT. The annual meeting will be held entirely online and you will be able to attend and participate by visiting <http://www.virtualshareholdermeeting.com/LXRX2022>, where you will be able to vote electronically and submit questions. You will not be able to attend the annual meeting in person. We are taking measures so that our stockholders may still meaningfully participate in the annual meeting notwithstanding the virtual platform. You will need the 16-digit control number included with these proxy materials to attend the annual meeting.

Your vote is important, regardless of the number of shares that you hold. Whether or not you plan to attend the annual meeting, I hope you will vote as soon as possible, either electronically on the Internet, by telephone or by signing and returning the enclosed proxy card. You can revoke any prior proxy by attending the annual meeting and voting electronically during the meeting or by otherwise revoking your proxy as described in the proxy statement.

Thank you for your ongoing support of and continued interest in Lexicon Pharmaceuticals.

Sincerely,

/s/ Lonnel Coats

Lonnel Coats
Chief Executive Officer

LEXICON PHARMACEUTICALS, INC.
2445 Technology Forest Blvd., 11th Floor
The Woodlands, Texas 77381
(281) 863-3000

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS
TO BE HELD MAY 20, 2022

TO OUR STOCKHOLDERS:

The annual meeting of stockholders of Lexicon Pharmaceuticals, Inc. will be held on Friday, May 20, 2022 at 8:00 a.m. CDT. The annual meeting will be held entirely online at <http://www.virtualshareholdermeeting.com/LXRX2022>. At the annual meeting, stockholders will consider and vote on the following matters:

- the election of the three Class I directors named in this proxy statement;
- a proposal to ratify and approve the Third Amended and Restated Certificate of Incorporation increasing the number of authorized shares of our common stock from 225,000,000 to 300,000,000;
- an advisory vote to approve the compensation paid to our named executive officers;
- a proposal to ratify and approve the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2022; and
- acting on any other business that properly comes before the annual meeting.

You are entitled to vote at the annual meeting only if you are the record owner of shares of our common stock at the close of business on March 22, 2022.

It is important that your shares be represented at the annual meeting whether or not you plan to attend online. **Please cast your vote electronically on the Internet, by telephone or by signing and returning the enclosed proxy card as promptly as possible.** If you attend the annual meeting online, and wish to do so, you may revoke the proxy and vote online at the annual meeting.

By order of the board of directors,

/s/ Brian T. Crum

Brian T. Crum
Secretary

The Woodlands, Texas
April 8, 2022

LEXICON PHARMACEUTICALS, INC.
2445 Technology Forest Blvd., 11th Floor
The Woodlands, Texas 77381
(281) 863-3000

PROXY STATEMENT
FOR
ANNUAL MEETING OF STOCKHOLDERS

To Be Held May 20, 2022

GENERAL INFORMATION

Purpose of this Proxy Statement

We have prepared this proxy statement to solicit proxies on behalf of our board of directors for use at our 2022 annual meeting of stockholders and any adjournment or postponement of such meeting.

Notice of Internet Availability of Proxy Materials

As permitted by rules adopted by the Securities and Exchange Commission, we are providing access to our proxy materials over the Internet. Accordingly, beginning on April 8, 2022, we are mailing to our stockholders a notice containing instructions on how to access our proxy materials, including our proxy statement and annual report, and vote electronically over the Internet. The notice also provides instructions on how stockholders may request a paper copy of our proxy materials free of charge. Our proxy materials may be accessed by stockholders at any time after the date of mailing of the notice.

Date, Time and Place of Annual Meeting

The annual meeting will be held on Friday, May 20, 2022 at 8:00 a.m. CDT. The annual meeting will be held entirely online at <http://www.virtualshareholdermeeting.com/LRX2022>.

We believe that the online format facilitates stockholder attendance and participation by leveraging technology to allow us to communicate in a safe, effective and efficient manner with our stockholders. This online format also empowers stockholders around the world to participate at no cost. We have designed the online format to enhance stockholder access and participation and protect stockholder rights by, among other things, providing stockholders multiple opportunities to submit questions for the annual meeting and offering live technical support for all stockholders attending the annual meeting online.

In order to attend the annual meeting, you should use the control number provided on your proxy card or notice of Internet availability of proxy materials. If your shares are held by an intermediary, such as a broker or bank, instructions for attending the annual meeting should also be provided on the voting instruction card provided by such intermediary.

Matters to Be Considered at the Annual Meeting

At the annual meeting, our stockholders will be asked to consider and act upon the following matters:

- the election of the three Class I directors named in this proxy statement;
- a proposal to ratify and approve the Third Amended and Restated Certificate of Incorporation increasing the number of authorized shares of our common stock from 225,000,000 to 300,000,000;
- an advisory vote to approve the compensation paid to our named executive officers; and
- a proposal to ratify and approve the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2022.

Our board of directors does not intend to bring any other matters before the annual meeting and has not been informed that any other matters are to be presented by others. Our bylaws contain several requirements that must be satisfied in order for any of our stockholders to bring a proposal before one of our annual meetings, including a requirement of delivering proper advance notice to us. Stockholders are advised to review our bylaws if they intend to present a proposal at any of our annual meetings.

Shares Entitled to Vote

You are entitled to vote at the annual meeting and at any postponement or adjournment thereof if you were the record owner of shares of our common stock as of the close of business on March 22, 2022, the record date for the annual meeting established by our board of directors. On the record date, 149,593,551 shares of our common stock were outstanding. If you were the record owner of shares of our common stock on the record date, you will be entitled to one vote for each share of stock that you own on each matter that is called to vote at the annual meeting or at any postponement or adjournment thereof.

Quorum

We must have a quorum to conduct any business at the annual meeting. This means that at least a majority of our outstanding shares eligible to vote at the annual meeting must be represented at the annual meeting, either in person during the annual meeting or by proxy. Cast abstentions are counted for purposes of determining whether a quorum is present. In addition, shares held by intermediaries that are voted for at least one matter at the annual meeting will be counted as being present for purposes of determining a quorum for all matters. This is true even if the beneficial owner's discretion has been withheld for voting on some or all other matters (commonly referred to as a "broker non-vote").

Vote Necessary to Approve Proposals

Our Class I directors will be elected by a plurality vote. As a result, the three persons receiving the greatest number of votes will be elected to serve as our Class I directors. Withholding authority to vote for a director nominee will not affect the outcome of the election of directors.

The ratification and approval of our Third Amended and Restated Certificate of Incorporation will require the affirmative vote of a majority of the common stock outstanding and entitled to vote thereon. Any abstention from voting or broker non-vote with respect to such matter will have the same effect as a vote against the proposal.

The approval on an advisory basis of the compensation paid to our named executive officers will require the affirmative vote of the majority of the votes cast with respect to such matter. Any abstention from voting or broker non-vote with respect to such matter will not count as a vote for or against the compensation paid to our named executive officers and will not affect the outcome of the advisory vote.

The ratification and approval of the appointment of Ernst & Young LLP as our independent auditors for the year ending December 31, 2022 will require the affirmative vote of a majority of the votes cast with respect to such matter. Any abstention from voting or broker non-vote with respect to such matter will not count as a vote for or against the appointment of Ernst & Young LLP and will not affect the outcome of the proposal.

Any other business that may properly come before the annual meeting for a vote will require the affirmative vote of a majority of the votes cast with respect to such matter unless a greater vote is required by law or our charter or bylaws. Any abstention or broker non-vote with respect to any such matter will not count as a vote for or against the proposal and will not affect the outcome of the proposal.

How to Vote Your Shares

You may vote online during the annual meeting at <http://www.virtualshareholdermeeting.com/LXRX2022> or by proxy. To ensure that your shares are represented at the annual meeting, we recommend you vote by proxy even if you plan to attend the annual meeting online. Even if you vote by proxy, if you wish, you can revoke your proxy and vote online at the annual meeting. If you want to vote at the annual meeting but your shares are held by an intermediary, such as a broker or bank, you will need to obtain from the intermediary either proof of your ownership of such shares as of March 22, 2022 or a proxy from such intermediary authorizing you to vote your shares at the meeting.

You may receive more than one proxy depending on how you hold your shares. If you hold your shares through an intermediary, such as a broker or bank, you may receive materials from them asking you how you want your shares to be voted at the annual meeting.

How to Vote by Proxy

By Internet or Telephone. You may vote electronically on the Internet or by telephone by following the instructions contained on the notice of Internet availability of our proxy materials. If you hold your shares through an intermediary, such as a broker or bank, please follow the voting instructions contained on the voting card used by the intermediary.

By Mail. If you request a paper copy of our proxy materials, you may vote by mail by completing, dating and signing the proxy card provided and mailing it in the pre-addressed envelope enclosed with the paper copy of our proxy materials.

How Your Proxy Will Be Voted

Giving us your proxy means that you are authorizing us to vote your shares at the annual meeting and at any adjournment or postponement thereof in the manner you direct. You may vote for our nominees for election as Class I directors, or withhold your vote for any one or more of those nominees. You may vote for or against the ratification and approval of our Third Amended and Restated Certificate of Incorporation, the approval on an advisory basis of the compensation paid to our named executive officers and the ratification and approval of the appointment of Ernst & Young LLP as our independent auditors for the year ending December 31, 2022, or abstain from voting on those proposals.

If any of our nominees for election as Class I directors become unavailable for any reason before the election, we may reduce the number of directors serving on our board of directors, or our board of directors may designate substitute nominees, as necessary. We have no reason to believe that any of our nominees for election as Class I directors will be unavailable. If our board of directors designates any substitute nominees, the persons receiving your proxy will vote your shares for such substitute(s) if they are instructed to do so by our board of directors or, in the absence of any such instructions, in accordance with their own best judgment.

If you vote by proxy but do not specify how you want your shares voted, your shares will be voted in favor of our nominees for election as Class I directors, in favor of the ratification and approval of our Third Amended and Restated Certificate of Incorporation, in favor of the approval on an advisory basis of the compensation paid to our named executive officers, and in favor of the ratification and approval of the appointment of Ernst & Young LLP as our independent auditors for the year ending December 31, 2022.

If you vote by proxy and any additional business properly comes before the annual meeting, the persons receiving your proxy will vote your shares on those matters as instructed by our board of directors or, in the absence of any such instructions, in accordance with their own best judgment. As of the date of this proxy statement, we are not aware of any other matter to be raised at the annual meeting.

How to Revoke Your Proxy

You may revoke your proxy at any time before your shares are voted by providing our corporate secretary with either a new proxy with a later date or a written notice of your desire to revoke your proxy at the following address:

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

You may also revoke your proxy at any time prior to your shares having been voted by attending the annual meeting online and notifying the inspector of election of your desire to revoke your proxy. Your proxy will not automatically be revoked merely because you attend the annual meeting online.

Inspector of Election

Broadridge Financial Solutions, Inc. will count votes and provide a representative who will serve as an inspector of election for the annual meeting.

List of Stockholders Entitled to Vote

A list of our stockholders entitled to vote at the annual meeting will be available online for inspection during the annual meeting. The stockholder list will also be available for inspection for ten days prior to the annual meeting at our corporate offices located at 2445 Technology Forest Blvd., 11th Floor, The Woodlands, Texas. Any inspection of this list at our offices will need to be conducted during ordinary business hours. If you wish to conduct an inspection of the stockholder list, we request that you please contact our corporate secretary before coming to our offices.

Solicitation of Proxies and Expenses

We are asking for your proxy on behalf of our board of directors. We will bear the entire cost of preparing, printing and soliciting proxies. We will send notices of Internet availability of proxy materials and, if requested, paper copies of our proxy materials to all of our stockholders of record as of the record date and to all intermediaries, such as brokers and banks,

that held any of our shares on that date on behalf of others. These intermediaries will then forward the notices and, if requested, paper copies of our proxy materials to the beneficial owners of our shares, and we will reimburse them for their reasonable out-of-pocket expenses for forwarding such materials. Our directors, officers and employees may solicit proxies by mail, in person or by telephone or other electronic communication. Our directors, officers and employees will not receive additional compensation for their solicitation efforts, but they will be reimbursed for any out-of-pocket expenses they incur. No solicitation of proxies will be made by specially engaged employees or paid solicitors.

Householding

As permitted by rules adopted by the Securities and Exchange Commission, we are delivering a single notice of Internet availability of proxy materials, annual report and proxy statement, as applicable, to any household at which two or more stockholders reside if we believe the stockholders are members of the same family, unless otherwise instructed by one or more of the stockholders. We will promptly deliver separate copies of these documents upon the written or oral request of any stockholder at a shared address to which a single copy of the documents were delivered.

If your household received a single set of any of these documents, but you would prefer to receive your own copy, or if you share an address with another stockholder and together both of you would like to receive only a single set of these documents, please follow these instructions:

- If your shares are registered in your own name, please contact our transfer agent, Computershare Inc., and inform them of your request by calling them at (877) 854-4583 or writing them at P.O. Box 505000, Louisville, Kentucky 40233-5000 or 462 South 4th Street, Suite 1600, Louisville, Kentucky 40202 for overnight correspondence.
- If an intermediary, such as a broker or bank, holds your shares, please contact Broadridge and inform them of your request by calling them at (800) 542-1061 or writing them at Householding Department, 51 Mercedes Way, Edgewood, New York 11717. Be sure to include your name, the name of your brokerage firm and your account number.

Appraisal Rights

Appraisal rights are not available to our stockholders in connection with the matters to be considered at the annual meeting.

**PROPOSAL NUMBER 1:
ELECTION OF DIRECTORS**

Our board of directors, which currently has nine members, is divided or "classified" into three classes. Directors in each class are elected to hold office for a term ending on the date of the third annual meeting following the annual meeting at which they were elected. The current term of our Class I directors will expire at this annual meeting. The current terms of our Class II and Class III directors will expire at our 2023 and 2024 annual meetings of stockholders, respectively.

The board of directors has nominated and urges you to vote for the election of the individuals identified below, who have been nominated to serve as Class I directors until our 2025 annual meeting of stockholders or until their successors are duly elected and qualified. Each of these individuals is a member of our present board of directors. Your signed proxy will be voted for the nominees named below unless you specifically indicate on the proxy that you are withholding your vote.

Nominees for Class I Directors

The following individuals are nominated for election as Class I directors:

<u>Name</u>	<u>Age</u>	<u>Position with the Company</u>	<u>Year First Became a Director</u>
Raymond Debbane	67	Chairman of the Board of Directors (Class I)	2007
Robert J. Lefkowitz, M.D.	78	Director (Class I)	2001
Alan S. Nies, M.D.	84	Director (Class I)	2003

Raymond Debbane has been a director since August 2007 and became chairman of our board of directors in February 2012. Mr. Debbane is president and chief executive officer of The Invus Group, LLC, which he founded in New York in 1985 as the exclusive investment advisor of Benelux-based Artal Group S.A. Mr. Debbane serves as chairman of the board of directors of WW, Inc. and as chairman or director of a number of private companies in which Invus and Artal Group S.A. have invested. He previously served as a director of Blue Buffalo Pet Products, Inc. from 2007 until April 2018 when Blue Buffalo was acquired by General Mills, Inc. Before founding The Invus Group, Mr. Debbane was a manager in the Paris office of The Boston Consulting Group, Inc., where he did consulting work for a number of major European and international companies. Mr. Debbane holds an M.B.A. from Stanford University, an M.S. in food science and technology from the University of California at Davis, and a B.S. in agricultural sciences and agricultural engineering from American University of Beirut.

Mr. Debbane provides us with the benefit of his extensive financial markets and investment expertise gained in more than 30 years of leading the identification, selection, negotiation and oversight of a wide range of investments in his role as president and chief executive officer of The Invus Group, as well as his background in strategic consulting across a broad range of industries developed while with The Boston Consulting Group. Mr. Debbane is a designee of Invus, L.P. and its affiliates pursuant to our stockholders' agreement with Invus described under the heading "Transactions with Related Persons - Arrangements with Invus."

Robert J. Lefkowitz, M.D. has been a director since February 2001. Dr. Lefkowitz is the James B. Duke Professor of Medicine, professor of biochemistry and a Howard Hughes Medical Institute investigator at Duke University Medical Center, where he has served on the faculty since 1973. Dr. Lefkowitz is a member of the National Academy of Sciences and has received more than 50 major awards for his research, including the 2012 Nobel Prize in Chemistry, the Shaw Prize, the Albany Medical Center Prize and the 2007 National Medal of Science. Dr. Lefkowitz received his B.A. from Columbia University and his M.D. from Columbia University College of Physicians and Surgeons.

Dr. Lefkowitz provides us with the benefit of his medical expertise and his extensive experience in biological and pharmaceutical research, particularly with respect to the identification of drug targets and preclinical evaluation of drug candidates, gained in more than 40 years as a member of the faculty at Duke University Medical Center.

Alan S. Nies, M.D. has been a director since November 2003. Dr. Nies served in a series of senior management positions during ten years at Merck & Co. Inc. until his retirement in 2002, including senior vice president, clinical sciences. Prior to joining Merck, Dr. Nies spent fifteen years as professor of medicine and pharmacology and head of the Division of Clinical Pharmacology at the University of Colorado Health Sciences Center. Dr. Nies holds a B.S. from Stanford University and an M.D. from Harvard Medical School.

Dr. Nies provides us with the benefit of his extensive clinical development experience, particularly with respect to the design, management and reporting of clinical trials, as well as his organizational and management skills developed while serving in his various leadership positions with Merck and the University of Colorado Health Sciences Center.

The Board of Directors recommends that stockholders vote “FOR” the foregoing nominees for election as Class I directors.

Current and Continuing Directors

The current directors of the Company are identified below:

<u>Name</u>	<u>Age</u>	<u>Position with the Company</u>
Raymond Debbane ⁽³⁾	67	Chairman of the Board of Directors (Class I)
Philippe J. Amouyal ⁽²⁾	63	Director (Class III)
Samuel L. Barker, Ph.D. ⁽¹⁾⁽²⁾	79	Director (Class II)
Lonnell Coats	57	Chief Executive Officer and Director (Class III)
Robert J. Lefkowitz, M.D. ⁽³⁾	78	Director (Class I)
Alan S. Nies, M.D.	84	Director (Class I)
Frank P. Palantoni ⁽¹⁾⁽²⁾	64	Director (Class III)
Christopher J. Sobecki	63	Director (Class II)
Judith L. Swain, M.D. ⁽¹⁾⁽³⁾	73	Director (Class II)

⁽¹⁾ Member of the Audit Committee

⁽²⁾ Member of the Compensation Committee

⁽³⁾ Member of the Corporate Governance Committee

Information regarding the business experience of Mr. Debbane, Dr. Lefkowitz and Dr. Nies is set forth above under the heading “- Nominees for Class I Directors.”

Philippe J. Amouyal has been a director since August 2007 and is a managing director of The Invus Group, LLC, a position he has held since 1999. Previously, Mr. Amouyal was a vice president and director of The Boston Consulting Group, Inc. in Boston, Massachusetts, where he coordinated the global technology and electronics practice through most of the 1990s. Mr. Amouyal also serves as director at a number of private companies in which Invus has invested. He previously served as a director of WW, Inc. from 2002 until February 2019 and of Blue Buffalo Pet Products, Inc. from 2007 until April 2018 when Blue Buffalo was acquired by General Mills, Inc. Mr. Amouyal holds an M.S. in engineering and a DEA in management from Ecole Centrale de Paris and was a research fellow at the Center for Policy Alternatives of the Massachusetts Institute of Technology.

Mr. Amouyal provides us with the benefit of his broad business and financial experience, as well as his expertise in compensation and performance management and the assessment and prioritization of research and development projects, gained in his active participation in the identification, selection, negotiation and oversight of investments by The Invus Group and his consulting experience with The Boston Consulting Group. Mr. Amouyal is a designee of Invus, L.P. and its affiliates pursuant to our stockholders’ agreement with Invus described under the heading “Transactions with Related Persons - Arrangements with Invus.”

Samuel L. Barker, Ph.D. has been a director since March 2000 and served as chairman of our board of directors from 2005 to 2012. Dr. Barker previously co-founded and served as president and chief executive officer of Clearview Projects, Inc., a provider of partnering and transaction services to biopharmaceutical companies. Dr. Barker served in a series of leadership positions at Bristol-Myers Squibb Company until his retirement in 1999. His positions at Bristol-Myers Squibb included service as executive vice president, Worldwide Franchise Management and Strategy; president, United States Pharmaceuticals; and president, Bristol-Myers Squibb Intercontinental Commercial Operations. Dr. Barker also previously held executive positions in research and development, manufacturing, finance, business development and sales and marketing at Squibb Pharmaceuticals. Dr. Barker currently serves as a director of Cyclacel Pharmaceuticals, Inc. Dr. Barker received his B.S. from Henderson State College, his M.S. from the University of Arkansas and his Ph.D. from Purdue University.

Dr. Barker provides us with the benefit of his extensive experience in a wide variety of disciplines within the pharmaceutical industry, including the development and commercialization of pharmaceutical products, the identification, evaluation and negotiation of collaborative agreements, and the management of pharmaceutical marketing and sales efforts, as well as his organizational and management skills developed while serving in his various leadership positions at Bristol-Myers Squibb and Clearview Projects.

Lonnell Coats has been our chief executive officer and a director since July 2014. Mr. Coats previously served in a series of executive leadership positions at Eisai Inc. and Eisai Corporation of North America, where he worked for 18 years

before joining our company, most recently as chief executive officer from 2010 to 2014. Prior to joining Eisai, Mr. Coats spent eight years with Janssen Pharmaceuticals, Inc., a division of Johnson & Johnson, where he held a variety of management and sales positions. Mr. Coats serves as a director of Blueprint Medicines Corporation and holds a B.S. from Oakland University.

Mr. Coats provides us with the benefit of his extensive experience in a wide variety of disciplines within the pharmaceutical industry, including the development and commercialization of pharmaceutical products, the management of pharmaceutical marketing and sales efforts and the planning and execution of strategic initiatives, as well as his organizational and management skills developed while serving in his various leadership positions at Eisai.

Frank P. Palantoni has been a director since November 2004. Mr. Palantoni is chief executive officer of Laboratory M2, a clean technology company involved in animal health, crop protection and retail sectors. Mr. Palantoni was president of Palantoni & Partners LLC, an advisory firm for the consumer and health care industries, from 2013 to 2016. He previously served as president of the pet and animal health division of Central Garden & Pet Company, was a partner at P3 Capital Management LLC, an early stage consumer products equity fund, served as chief operating officer and chief executive officer of Prestige Brands Holding, Inc. and held a variety of senior management positions with Novartis AG, including president and chief executive officer, worldwide of the Gerber Products Company, and chief executive officer for North American operations of the Consumer Health Division. Prior to joining Novartis, he held a series of senior management positions with The Danone Group. Mr. Palantoni served as a director of Mondias Natural Products Inc. from 2017 until June 2020 and holds a B.S. from Tufts University and an M.B.A. from Columbia University.

Mr. Palantoni provides us with the benefit of his extensive business operations experience, as well as his expertise in compensation and performance management and his broad business and management skills developed while serving in his various leadership positions in the consumer health products industry.

Christopher J. Sobecki has been a director since August 2007 and is a managing director of The Invus Group, LLC, which he joined in 1989. Mr. Sobecki is currently a director of WW, Inc., as well as a number of private companies in which Invus has invested. He holds a B.S. in industrial engineering from Purdue University and an M.B.A. from Harvard University.

Mr. Sobecki provides us with the benefit of his diversified business and financial experience, including a particular expertise in risk assessment and business strategy development, and relationships in the financial community gained in his active participation in the identification, selection, negotiation and oversight of investments by The Invus Group and his service as a director of public and private companies. Mr. Sobecki is a designee of Invus, L.P. and its affiliates pursuant to our stockholders' agreement with Invus described under the heading "Transactions with Related Persons - Arrangements with Invus."

Judith L. Swain, M.D. has been a director since September 2007. Dr. Swain is a visiting professor of medicine at the National University of Singapore and chief medical officer of Physiowave, Inc. She previously served as founding director of the Singapore Institute for Clinical Sciences, dean for translational medicine at the University of California, San Diego, chair of the Department of Medicine at Stanford University, and on the medical faculties of the University of Pennsylvania and Duke University. She has previously served in a number of national and international leadership roles and as a director or member of the scientific advisory boards for a number of biomedical technology companies and is co-founder of Synecor, LLC. Dr. Swain has served as a director of Prometheus Biosciences, Inc. since February 2021. Dr. Swain received her B.S. from the University of California, Los Angeles and her M.D. from the University of California, San Diego.

Dr. Swain provides us with the benefit of her extensive medical and scientific research experience gained in her more than 30 years as a practicing physician and research scientist, as well as her organizational and management skills developed in her numerous leadership positions with a variety of prominent research and academic institutions.

**PROPOSAL NUMBER 2:
RATIFICATION AND APPROVAL OF THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION**

Our board of directors believes that it is advisable to ratify and approve our Third Amended and Restated Certificate of Incorporation increasing the number of authorized shares of our common stock from 225,000,000 shares to 300,000,000 shares. As of March 22, 2022, of the 225,000,000 shares of our common stock authorized by our Second Amended and Restated Certificate of Incorporation, 149,593,551 shares were issued and outstanding, 488,205 shares were issued and held in treasury, 23,289,376 shares were reserved for issuance under our equity incentive plans and 420,673 shares were reserved for issuance under outstanding warrants. After the proposed increase in the number of authorized shares of our common stock to 300,000,000 shares, 126,208,195 shares of our common stock would be authorized but not issued or reserved for issuance.

Our board of directors believes that the increase in the number of authorized shares of our common stock will provide us with greater flexibility in effecting future acquisitions and financings without the delay and expense associated with obtaining the approval or consent of our stockholders at the same time the shares are needed. We expect that our future growth may require the use of our common stock from time to time either as consideration for acquisitions or as part of a financing for us either through the use of our common stock or securities convertible into our common stock. Such shares may be issued in conjunction with both public offerings and private placements of shares of our common stock, which issuances, depending on the circumstances, may or may not require future stockholder approval under the rules of The Nasdaq Global Select Market. Such shares could also be used for our equity compensation plans, subject to appropriate stockholder approval. We do not have any current plans, proposals or understandings that would require the use of the additional authorized shares of our common stock to be issued.

Each additional authorized share of common stock would have the same rights and privileges as each share of currently authorized common stock. Under our Second Amended and Restated Certificate of Incorporation, holders of 20% or more of our issued and outstanding common stock, including Invus, L.P. and its affiliates based on their current ownership interest in our common stock, have preemptive rights to purchase additional shares of our common stock. Such preemptive rights would not be affected or modified by the Third Amended and Restated Certificate of Incorporation.

Accordingly, we are asking that stockholders ratify and approve the Third Amended and Restated Certificate of Incorporation, the complete text of which is set forth in Appendix A to this proxy statement. As Invus, L.P. and its affiliates currently own approximately 50.5% of our outstanding common stock, no additional votes will be required to ratify and approve the Third Amended and Restated Certificate of Incorporation if Invus, L.P. and its affiliates vote in favor of this proposal. The Third Amended and Restated Certificate of Incorporation was approved by our board of directors, subject to stockholder approval, on February 10, 2022.

If the Third Amended and Restated Certificate of Incorporation is approved by the requisite vote of stockholders, we will file the Third Amended and Restated Certificate of Incorporation with the Delaware Secretary of State as soon as reasonably practicable after the annual meeting and it will become effective upon such filing.

The Board of Directors recommends that stockholders vote “FOR” the ratification and approval of the Third Amended and Restated Certificate of Incorporation.

**PROPOSAL NUMBER 3:
ADVISORY VOTE TO APPROVE COMPENSATION PAID TO NAMED EXECUTIVE OFFICERS**

Section 14A of the Securities and Exchange Act of 1934, as amended, requires that we provide our stockholders with an opportunity to vote, on a non-binding and advisory basis, on the compensation of our named executive officers, as disclosed in this proxy statement in accordance with the compensation disclosure rules of the Securities and Exchange Commission.

As described below under “Executive and Director Compensation - Compensation Discussion and Analysis,” we have developed a compensation policy that is designed to attract and retain key executives responsible for our success and motivate management to enhance long-term stockholder value. We believe our compensation policy strikes an appropriate balance between the implementation of responsible, measured compensation practices and the effective provision of incentives for our named executive officers to exert maximum efforts for our success.

Accordingly, we ask our stockholders to vote on the following resolution at the annual meeting:

“RESOLVED, that the Company’s stockholders hereby approve, on an advisory basis, the compensation of the named executive officers, as disclosed in the Company’s proxy statement for the 2022 annual meeting of stockholders pursuant to the compensation disclosure rules of the Securities and Exchange Commission, including the Compensation Discussion and Analysis, 2021 Summary Compensation Table and the other compensation related tables and disclosure.”

As this vote is advisory, it will not be binding upon the board of directors or the compensation committee and neither the board of directors nor the compensation committee will be required to take any action as a result of the outcome of this vote. However, the compensation committee will carefully consider the outcome of this vote when considering future executive compensation policies.

The Board of Directors recommends that stockholders vote “FOR” the approval, on an advisory basis, of the compensation paid to our named executive officers, as disclosed in this proxy statement.

**PROPOSAL NUMBER 4:
RATIFICATION AND APPROVAL OF INDEPENDENT AUDITORS**

The board of directors has appointed the firm of Ernst & Young LLP as our independent auditors to make an examination of our accounts for the fiscal year ending December 31, 2022, subject to ratification by our stockholders. Representatives of Ernst & Young LLP, are expected to be present at the annual meeting, will have an opportunity to make a statement if they desire to do so and are expected to be available to respond to appropriate questions.

The Board of Directors recommends that stockholders vote "FOR" ratification and approval of the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2022.

Compensation of Independent Auditors

The following table presents the estimated aggregate fees billed and to be billed by Ernst & Young LLP for services performed during our last two fiscal years.

	Years Ended December 31,	
	2021	2020
Audit fees ⁽¹⁾	\$ 560,000	\$ 696,000
Audit-related fees ⁽²⁾	32,800	32,800
Tax fees	—	—
All other fees	—	—
	<u>\$ 592,800</u>	<u>\$ 728,800</u>

⁽¹⁾ "Audit fees" include professional services rendered for (i) the audit of our internal control over financial reporting, as required by the Sarbanes-Oxley Act of 2002, for the fiscal years ended December 31, 2020 and 2021, (ii) the audit of our annual financial statements for the fiscal years ended December 31, 2020 and 2021, (iii) the reviews of the financial statements included in our quarterly reports on Form 10-Q for such years and (iv) the issuance of consents and other matters relating to registration statements filed by us.

⁽²⁾ "Audit-related fees" include assurance or related services reasonably related to our audit for the fiscal years ended December 31, 2020 and 2021. These fees related to the audit of the financial statements of our 401(k) plan.

The audit committee reviewed and approved all the fees described above. As part of its duties, the audit committee has determined that the provision by Ernst & Young LLP of the services described above is compatible with maintaining the auditors' independence.

Audit Committee Pre-Approval Policies and Procedures

The audit committee has adopted policies and procedures requiring the pre-approval of all audit and non-audit services rendered by our independent auditors, either as part of the audit committee's approval of the scope of the engagement of the independent auditors or on a case-by-case basis before the independent auditors are engaged to provide each service. The audit committee's pre-approval authority may be delegated to one or more of its members, but any pre-approval decision must be reported to the full audit committee at its next regularly scheduled meeting.

Audit Committee Report

The role of the audit committee is to assist the board of directors in its oversight of our financial reporting process. The audit committee reviews our internal accounting procedures and consults with, and reviews the services provided by, our independent auditors.

The management of our company is responsible for the preparation, presentation and integrity of our financial statements, our accounting and financial reporting principles and internal controls and procedures designed to assure compliance with the accounting standards and applicable laws and regulations. Our independent auditors are responsible for auditing our financial statements and expressing an opinion as to their conformity with generally accepted accounting principles.

In the performance of its oversight function, the audit committee has reviewed and discussed the audited financial statements with management. The committee has also discussed with our independent auditors the matters required to be discussed by PCAOB Auditing Standard No. 1301, *Communications with Audit Committees*, as currently in effect. Finally, the committee has received the written disclosures and the letter from our independent auditors required by the applicable requirements of the Public Company Accounting Oversight Board regarding our independent auditors' communications with

the audit committee concerning independence, as currently in effect, and has discussed with our independent auditors their independence.

Based upon the review and discussions described in this report, and subject to the limitations on the role and responsibilities of the audit committee referred to in the audit committee charter, the audit committee recommended to the board of directors that the audited financial statements be included in our annual report on Form 10-K for the year ended December 31, 2021.

Audit Committee

Samuel L. Barker, Ph.D. (Chairman)
Frank P. Palantoni
Judith L. Swain, M.D.

The foregoing audit committee report shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference by any general statement incorporating by reference this proxy statement into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate this audit committee report by reference, and shall not otherwise be deemed filed under such acts.

STOCK OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table presents information regarding the beneficial ownership of our common stock as of March 22, 2022 by:

- each of the individuals listed in “Executive and Director Compensation - Summary Compensation Table for 2021”;
- each of our directors and nominees
- each person, or group of affiliated persons, who is known by us to own beneficially more than five percent of our common stock; and
- all current directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission computing the number of shares beneficially owned by a person and the percentage ownership of that person. Shares of common stock underlying stock options held by that person that are currently exercisable or exercisable within 60 days of March 22, 2022 and restricted stock units held by that person that are scheduled to vest within 60 days of March 22, 2022 are considered outstanding. These shares, however, are not considered outstanding when computing the percentage ownership of each other person.

Except as indicated in the footnotes to this table and pursuant to state community property laws, each stockholder named in the table has sole voting and investment power for the shares shown as beneficially owned by them. Percentage of ownership is based on 149,593,551 shares of common stock outstanding on March 22, 2022. Unless otherwise indicated in the footnotes, the address of each of the individuals named below is: c/o Lexicon Pharmaceuticals, Inc., 2445 Technology Forest Blvd., 11th Floor, The Woodlands, Texas 77381.

	Number of Shares Beneficially Owned	Beneficial Ownership	
		Shares Issuable Pursuant to Options Exercisable or Restricted Stock Units Scheduled to Vest within 60 Days of March 22, 2022	Percentage Ownership
5% Stockholders			
Invus, L.P., Invus Public Equities, L.P., Invus Partners, LLC and Artal International S.C.A. ⁽¹⁾	75,499,578	—	50.5 %
Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P. and Biotechnology Value Trading Fund OS LP and BVF Partners L.P. ⁽²⁾	14,360,000	—	9.6 %
Directors and Named Executive Officers			
Lonnell Coats	586,003	1,608,448	1.5 %
Jeffrey L. Wade	193,680	675,056	*
Brian T. Crum	99,458	273,972	*
Craig B. Granowitz, M.D., Ph.D.	—	—	*
Alan J. Main, Ph.D.	175,589	584,633	*
Raymond Debbane ⁽³⁾	4,648,735	44,777	3.1 %
Philippe J. Amouyal	27,006	44,777	*
Samuel L. Barker, Ph.D.	66,291	44,777	*
Robert J. Lefkowitz, M.D.	27,006	44,777	*
Alan S. Nies, M.D.	27,720	44,777	*
Frank P. Palantoni	27,006	44,777	*
Christopher J. Sobocki	145,697	44,777	*
Judith L. Swain, M.D.	27,006	44,777	*
All current directors and executive officers as a group ⁽³⁾ (17 persons)	6,175,884	3,864,276	6.5 %

* Represents beneficial ownership of less than 1 percent.

- ⁽¹⁾ Based upon a Schedule 13D/A filed with the SEC on January 21, 2021, reflecting the beneficial ownership of our common stock by Invus, L.P., Invus Public Equities, L.P., Invus Partners, LLC, Artal International S.C.A. and related parties. Invus, L.P. and related parties may be deemed to have sole investment and voting power with respect to 35,402,689 of such shares and shared voting power with respect to 3,516,214 of such shares. Invus Public Equities, L.P. and related parties may be deemed to have sole investment and shared voting power with respect to 3,516,214 of such shares. Invus Partners, LLC and related parties may be deemed to have sole investment and voting power with respect to 4,321,214 of such shares. Artal International S.C.A. and related parties may be deemed to have sole investment and voting power with respect to 71,178,364 of such shares. The address for Invus, L.P., Invus Public Equities, L.P. and Invus Partners, LLC is c/o The Invus Group, LLC, 750 Lexington Avenue, 30th Floor, New York, New York 10022. The address for Artal International S.C.A. is 44, Rue De La Vallée, L-2661, Luxembourg, Luxembourg.
- ⁽²⁾ Based upon a Schedule 13G/A filed with the SEC on February 14, 2022, reflecting the beneficial ownership of our common stock by Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P., Biotechnology Value Trading Fund OS LP and BVF Partners L.P. Biotechnology Value Fund, L.P. and related parties may be deemed to have shared investment and voting power with respect to 7,557,501 of such shares. Biotechnology Value Fund II, L.P. and related parties may be deemed to have shared investment and voting power with respect to 5,665,077 of such shares. Biotechnology Value Trading Fund OS LP and related parties may be deemed to have shared investment and voting power with respect to 869,596 of such shares. BVF Partners L.P. and related parties may be deemed to have shared investment and voting power with respect to the 14,092,174 shares beneficially owned by Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P. and Biotechnology Value Trading Fund OS LP, as well as 267,826 additional shares. The address for Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P. and BVF Partners L.P. is 44 Montgomery St., 40th Floor, San Francisco, California 94104. The address for Biotechnology Value Trading Fund OS LP and BVF Partners L.P. is P.O. Box 309 Ugland House, Grand Cayman KY1-1104, Cayman Islands.
- ⁽³⁾ Includes 4,321,214 shares beneficially owned by Invus Partners, LLC and related parties. Mr. Debbane disclaims beneficial ownership of these shares.

EQUITY COMPENSATION PLAN INFORMATION

The following table presents aggregate summary information as of December 31, 2021 regarding the common stock that may be issued upon exercise of options, warrants and rights under our 2017 Equity Incentive Plan and 2017 Non-Employee Directors' Equity Incentive Plan.

Plan Category	(a)	(b)	(c)
	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted average exercise price per share of outstanding options, warrants and rights ⁽²⁾	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders ⁽¹⁾	10,221,278	\$ 6.8029	14,048,092
Equity compensation plans not approved by security holders	—	—	—
Total	10,221,278	\$ 6.8029	14,048,092

⁽¹⁾ Consists of shares of our common stock issuable upon the exercise of outstanding stock options or vesting of outstanding restricted stock units granted under our 2017 Equity Incentive Plan and 2017 Non-Employee Directors' Equity Incentive Plan or remaining available for issuance under those plans.

⁽²⁾ Reflects only the weighted-average exercise price per share of outstanding stock options granted under our 2017 Equity Incentive Plan and 2017 Non-Employee Directors' Equity Incentive Plan and excludes from such calculation 1,822,043 restricted stock units granted under our 2017 Equity Incentive Plan pursuant to which shares of our common stock may be issued for no additional consideration.

CORPORATE GOVERNANCE

Independence of the Board of Directors

After reviewing all relevant transactions and relationships involving each member of the board of directors (and his or her family), the board of directors has affirmatively determined that Raymond Debbane, Philippe J. Amouyal, Samuel L. Barker, Ph.D., Robert J. Lefkowitz, M.D., Alan S. Nies, M.D., Frank P. Palantoni, Christopher J. Sobecki and Judith L. Swain, M.D., which members constitute a majority of the board of directors, are “independent” in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc. In making such determinations, the board of directors considered the percentage of our outstanding common stock owned by Invus and its affiliates and the effect of such ownership on the independence of Mr. Debbane, Mr. Amouyal and Mr. Sobecki.

Board Committees

Audit Committee. Our audit committee has been established in accordance with Section 3(a)(58)(A) of the Securities Exchange Act of 1934 to oversee our accounting and financial reporting processes and the audits of our financial statements. In that regard, the audit committee assists our board of directors in monitoring the integrity of our financial statements, the qualifications, independence and performance of our independent auditors and our compliance with legal and regulatory requirements. The audit committee operates pursuant to a charter that was last amended and restated by the board of directors on July 27, 2017, a copy of which appears on our website at www.lexpharma.com under the caption “Investors - Corporate Governance.”

The current members of our audit committee are Samuel L. Barker, Ph.D. (chair), Frank P. Palantoni and Judith L. Swain, M.D. The board of directors, in its business judgment, has determined that Dr. Barker, Mr. Palantoni and Dr. Swain are “independent” in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc. The board of directors, in its business judgment, has also determined that Samuel L. Barker, Ph.D. is an “audit committee financial expert” as defined in Item 407(d)(5) of Regulation S-K.

Compensation Committee. Our compensation committee has been established to oversee the compensation of our employees, including our chief executive officer and other officers. The compensation committee also has responsibility for the evaluation and approval of all compensation plans, policies and programs, including the issuance of stock options, restricted stock units and other awards under our 2017 Equity Incentive Plan. The compensation committee operates pursuant to a charter that was last amended and restated by the board of directors on February 7, 2019, a copy of which appears on our website at www.lexpharma.com under the caption “Investors - Corporate Governance.”

The compensation committee may delegate any of its authority to subcommittees consisting of one or more compensation committee members, with all subcommittee decisions being presented to the full compensation committee at its next scheduled meeting. The compensation committee did not delegate any such authority with respect to 2021 compensation matters.

The compensation committee may retain compensation consultants, legal counsel or other advisors when it deems appropriate to assist in its evaluation of executive compensation. The compensation committee has engaged Pearl Meyer & Partners, LLC as independent compensation consultants as described under the heading “Executive and Director Compensation - Compensation Discussion and Analysis.”

The compensation committee meets in connection with most regularly scheduled meetings of the board of directors, and holds meetings after the commencement of each year specifically devoted to evaluating corporate and individual performance during the prior year and making compensation decisions on such basis. In preparation for such decisions, our chief executive officer generally reviews the performance of officers other than himself and, in consultation with the compensation committee and at its direction, makes certain recommendations to the compensation committee relating to their compensation. The compensation committee reviews such recommendations and makes changes to such recommendations as it deems appropriate. All executive compensation determinations are made by the compensation committee independently from management.

The current members of our compensation committee are Mr. Palantoni (chair), Philippe J. Amouyal and Samuel L. Barker, Ph.D. The board of directors, in its business judgment, has determined that Mr. Palantoni, Mr. Amouyal and Dr. Barker are “independent” in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc. In making such determinations, the board of directors considered the matters relating to Mr. Amouyal described under the heading “Corporate Governance - Independence of the Board of Directors.”

Corporate Governance Committee. Our corporate governance committee has been established to oversee all aspects of our corporate governance functions. In that regard, the corporate governance committee makes recommendations to the board of directors regarding the identification, evaluation and selection of candidates to serve on the board of directors, the composition of board committees and the development of other corporate governance functions. The corporate governance committee operates pursuant to a charter that was last amended and restated by the board of directors on February 7, 2013, a copy of which appears on our website at www.lexpharma.com under the caption "Investors - Corporate Governance."

The corporate governance committee has not established any specific minimum qualifications for membership on our board of directors. Rather, the committee will generally consider all relevant factors, which may include independence, experience, diversity, leadership qualities and strength of character. As the corporate governance committee does not uniquely consider diversity relative to the other factors, the committee has not established a policy with regard to the consideration of diversity in identifying potential director candidates. The corporate governance committee uses its available network of contacts when compiling a list of potential director candidates and may also engage outside consultants when appropriate. The committee also considers potential director candidates recommended by stockholders and other parties and all potential director candidates are evaluated based on the above criteria. Because the corporate governance committee makes no distinction in its evaluation of candidates based on whether such candidates are recommended by stockholders or other parties, no formal policy or procedure has been established for the consideration of director candidates recommended by stockholders.

Any stockholder wishing to propose a potential director candidate may submit a recommendation in writing within the time frame specified in our bylaws. All such communications should be sent to 2445 Technology Forest Blvd., 11th Floor, The Woodlands, Texas 77381, Attn: Corporate Governance Committee. Submissions should include the full name of the proposed candidate and a detailed description of the candidate's qualifications, business experience and other relevant biographical information.

The current members of our corporate governance committee are Raymond Debbane (chair), Robert J. Lefkowitz, M.D. and Judith L. Swain, M.D. The board of directors, in its business judgment, has determined that Mr. Debbane, Dr. Lefkowitz and Dr. Swain are "independent" in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc. In making such determinations, the board of directors considered the matters relating to Mr. Debbane described under the heading "Corporate Governance - Independence of the Board of Directors."

Board Diversity

Diversity is among the relevant factors considered by our board of directors and corporate governance committee for membership on our board of directors. The table below provides certain highlights relating the composition and diversity of our board of directors. Each of the categories listed in the below table has the meaning used in Nasdaq Listing Rule 5605(f).

Board Diversity Matrix (As of March 22, 2022)

Total Number of Directors	9			
	Female	Male	Non-Binary	Did not Disclose Gender
Directors	1	8	-	-
Number of Directors who identify in Any of the Categories Below:				
African American or Black	-	1	-	-
Alaskan Native or Native American	-	-	-	-
Asian	-	-	-	-
Hispanic or Latinx	-	-	-	-
Native Hawaiian or Pacific Islander	-	-	-	-
White	1	7	-	-
Two or More Races or Ethnicities	-	-	-	-
LGBTQ+		-		
Did not Disclose Demographic Background		-		

Board Leadership Structure and Role in Risk Oversight

The current leadership structure of our board of directors reflects a separation of the roles of chairman and principal executive officer. This leadership structure is intended to provide our board of directors with an appropriate level of independence from management and encourage a high degree of autonomy within our board of directors.

Our board of directors administers its risk oversight responsibilities by evaluating the material risks, including operational risks and liquidity risks, facing our company or inherent in our corporate strategy. This is accomplished through regular discussions with management and by reference to the independent understanding and knowledge of many such risks possessed by members of our board of directors. Our board of directors regularly reviews the viability and prudence of our corporate strategy in light of the evolving nature of such risks and makes adjustments to that strategy when appropriate. Our board of directors oversees management's implementation of our corporate strategy, remains alert for excessive risk-taking in such implementation and provides timely input to management regarding any critical risk issues. The efforts of our board of directors to oversee any risks relating to our financial reporting or internal accounting procedures are supplemented by the regular interactions of our audit committee with the individuals with day-to-day responsibilities for such functions.

Board and Committee Meetings and Attendance in 2021

In 2021, the board of directors met five times and took certain additional actions by unanimous written consent, the audit committee met five times, the compensation committee met six times and took certain additional actions by unanimous written consent and the corporate governance committee met two times. During 2021, none of our incumbent directors attended fewer than 75 percent of the aggregate number of meetings of the board of directors and committees during the period served.

It is our policy to encourage the members of our board of directors to attend all annual meetings of stockholders. All nine members of our board of directors attended our 2021 annual meeting of stockholders.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our directors, officers and employees, the text of which appears on our website at www.lexpharma.com under the caption "Investors - Corporate Governance." We intend to disclose on our website the nature of any amendment to or waiver from our code of business conduct and ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions within four business days following the date of such amendment or waiver. In the case of any such waiver, including an implicit waiver, we also intend to disclose the name of the person to whom the waiver was granted and the date of the waiver. To date, we have not granted any waivers under our code of business conduct and ethics.

Hedging Policies and Practices

We have adopted a policy that prohibits our employees, officers and directors, or any of their designees, from purchasing financial instruments (including prepaid variable forward contracts, equity swaps, collars and exchange funds), or otherwise engaging in transactions that hedge or offset, or are designed to hedge or offset, any decrease in the market value of any of our securities. Such policy also provides that such individuals should not engage in the trading of options to purchase or sell our securities.

Corporate Governance Guidelines

We have adopted corporate governance guidelines, including, among other things, guidelines with respect to the structure of our board of directors, director selection and qualifications, and non-employee director compensation. The text of our corporate governance guidelines appears on our website at www.lexpharma.com under the caption "Investors - Corporate Governance."

Stockholder Communications with the Board of Directors

We believe that our stockholders are currently provided a reasonable means to communicate with our board of directors and individual directors. As a result, our board of directors has not established a formal process for stockholders to send communications to the board of directors or individual directors. However, the corporate governance committee will consider, from time to time, whether adoption of a formal process for such stockholder communications has become necessary or appropriate. Stockholders may send communications to the board of directors or individual directors by mail at 2445 Technology Forest Blvd., 11th Floor, The Woodlands, Texas 77381, Attn: Board of Directors or any individual director.

Compensation Committee Interlocks and Insider Participation

During 2021, Frank P. Palantoni, Philippe J. Amouyal and Samuel L. Barker, Ph.D. served as members of the compensation committee of our board of directors. Mr. Amouyal is a designee of Invus pursuant to our stockholders' agreement with Invus, L.P. described under the heading "Transactions with Related Persons - Arrangements with Invus." During 2021, none of our executive officers served as a member of the board of directors or compensation committee of another entity, one of whose executive officers served as a member of our board of directors or compensation committee.

TRANSACTIONS WITH RELATED PERSONS

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. Invus, L.P. and its affiliates, which we collectively refer to as Invus, have subsequently made additional investments in our common stock and currently own approximately 50.5% of our outstanding common stock.

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 has 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 steps in accordance with our obligations under the stockholders' agreement to (1) 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 (2) 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 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 to 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. Invus possesses such preemptive and consent rights based on its current ownership interest in our common stock.

Related Party Transaction Policies

We have adopted written policies and procedures for the review, approval and ratification of interested transactions with related parties. Subject to certain exceptions provided in Item 404(a) of Regulation S-K, an "interested transaction" means any transaction, arrangement or relationship in which we are a participant and the amount involved will or may be expected to exceed \$120,000 in any calendar year, and in which any related party has or will have a direct or indirect material interest. A "related party" means (a) any executive officer, director, nominee for election as a director or any person beneficially owning five percent or more of our common stock and (b) any immediate family member of such parties.

All interested transactions are subject to the review and approval of our audit committee and if advance audit committee approval is not feasible, then the interested transaction will be considered for ratification at the audit committee's next regularly scheduled meeting. In determining whether to approve or ratify any interested transaction, the audit committee will consider, among other factors it may deem appropriate, whether the interested transaction is on terms no less favorable than terms generally available to an unaffiliated third party under similar circumstances and the extent of the related party's interest in the transaction. No director participates in any discussion or approval of an interested transaction for which he or she is a related party. On at least an annual basis, the audit committee reviews and assesses any ongoing interested transactions to ensure that the transaction remains appropriate.

EXECUTIVE AND DIRECTOR COMPENSATION

Compensation Discussion and Analysis

We have developed a compensation policy that is designed to attract and retain key executives responsible for our success and motivate management to enhance long-term stockholder value. All compensation decisions are made by our compensation committee pursuant to authority delegated by our board of directors. The annual compensation package for executive and other officers typically consists primarily of three elements:

- a base salary, which reflects the responsibilities relating to the position and individual performance;
- variable annual cash bonus awards, determined relative to pre-established bonus targets expressed as a percentage of base salary; and
- long-term stock-based incentive awards, designed to provide a continuing proprietary interest in our success.

We generally seek to set targeted total cash compensation, consisting of base salaries and annual cash bonus award targets, and total direct compensation, consisting of targeted total cash compensation and long-term stock-based incentive awards, at or near the median of a peer group of biopharmaceutical companies if such compensation level is justified by company performance, individual performance and prevailing financial conditions.

In determining peer group compensation, we use available data from a comprehensive survey of the compensation practices of several hundred companies in the biopharmaceutical industry. We expand on this survey data with reviews of the publicly-disclosed compensation practices of a group of biopharmaceutical companies selected for comparison purposes based on one or more factors, including market capitalization, revenues and stage of development.

For compensation decisions made in February 2019, this group of companies consisted of:

Acadia Pharmaceuticals Inc.	Blueprint Medicines Corporation	Intercept Pharmaceuticals, Inc.
Acceleron Pharma Inc.	Clovis Oncology, Inc.	MyoKardia, Inc.
Agiros Pharmaceuticals, Inc.	Corcept Therapeutics Incorporated	Portola Pharmaceuticals, Inc.
Arena Pharmaceuticals, Inc.	Enanta Pharmaceuticals, Inc.	Reata Pharmaceuticals, Inc.
Array Biopharma Inc.	Fibrogen, Inc.	Sangamo BioSciences, Inc.

For compensation decisions made in February 2020, this group of companies consisted of:

Acceleron Pharma Inc.	Denali Therapeutics Inc.	Omeros Corp
Aerie Pharmaceuticals, Inc.	Epizyme, Inc.	Portola Pharmaceuticals, Inc.
Agiros Pharmaceuticals, Inc.	Immunogen Inc	Principia Biopharma Inc.
Arena Pharmaceuticals, Inc.	Intercept Pharmaceuticals, Inc.	Radius Health, Inc.
Blueprint Medicines Corporation	Karyopharm Therapeutics Inc.	Sage Therapeutics, Inc.
Cara Therapeutics, Inc.	Molecular Templates, Inc.	Sangamo BioSciences, Inc.
Clovis Oncology, Inc.	MyoKardia, Inc.	Theravance Biopharma, Inc.
Cytokinetics Inc.	NGM Biopharmaceuticals Inc	

For compensation decisions made in February 2021, this group of companies consisted of:

Arbutus Biopharma Corporation	CytomX Therapeutics, Inc.	MEI Pharma, Inc.
Ardelyx, Inc.	Evelo Biosciences, Inc.	Molecular Templates, Inc.
Assembly Biosciences, Inc.	G1 Therapeutics, Inc.	Rigel Pharmaceuticals, Inc.
Athersys, Inc.	Jounce Therapeutics, Inc.	Solid Biosciences Inc.
Axcella Health Inc.	Kaleido Biosciences, Inc.	Syros Pharmaceuticals, Inc.

For compensation decisions made in February 2022, this group of companies consisted of:

Amarin Corporation plc	EyePoint Pharmaceuticals, Inc.	Omeros Corp
Cara Therapeutics, Inc.	G1 Therapeutics, Inc.	Radius Health, Inc.
Clovis Oncology, Inc.	Harmony Biosciences Holdings, Inc.	Rigel Pharmaceuticals, Inc.
Crinetics Pharmaceuticals, Inc.	Intercept Pharmaceuticals, Inc.	Sage Therapeutics, Inc.
Epizyme, Inc.	Karyopharm Therapeutics Inc.	Theravance Biopharma, Inc.

The peer group of biopharmaceutical companies for which we obtained survey data and the additional groups of companies listed above do not necessarily coincide with the companies comprising the Nasdaq Biotechnology Index. Although we acknowledge the inherent limitations in comparing our compensation practices with the compensation practices of these companies, we believe that these comparisons are useful and important points of reference in making compensation determinations.

In making compensation determinations and reviewing comparative data, the compensation committee reviews total direct compensation in its totality, assigning dollar values to each of the elements of such compensation, including base salary, annual cash bonus award targets and long-term stock-based incentive awards. The committee generally allocates a greater percentage of total direct compensation to long-term stock-based incentive awards in acknowledgment of the unique challenges present in the biopharmaceutical industry and in order to reinforce the alignment of interests between our executive and other officers and our stockholders.

In determining the level and composition of compensation of each of our executive and other officers, we take into account various qualitative and quantitative indicators of corporate and individual performance. In evaluating the performance of management, the compensation committee takes into consideration such factors as the commercial performance of our approved drug products, our efforts and preparations for regulatory approval and commercial launch of our drug candidates, the progress exhibited by our drug candidates in human clinical trials, the number and quality of drug candidates in clinical trials, the number and quality of preclinical drug candidates, the value and scope of strategic collaborations and alliances with leading pharmaceutical companies, and the ability to otherwise finance our operations from external sources. In addition, the compensation committee recognizes performance and achievements that are more difficult to quantify, such as the successful supervision of major corporate projects and demonstrated leadership ability.

The compensation committee generally makes executive compensation determinations in February of each year, taking into account both company and individual performance over the preceding year, as well as prevailing financial conditions. The compensation committee meets at least once in advance of the meeting in which executive compensation determinations are actually made to discuss considerations relating to those determinations.

The compensation committee may also retain compensation consultants, legal counsel or other advisors when it deems appropriate to assist in its evaluation of executive or director compensation. In February 2019, the compensation committee engaged Pearl Meyer & Partners, LLC as an independent compensation consultant to assess the market competitiveness of our non-employee director compensation and provide the compensation committee with recommendations based on such assessment. At the compensation committee's request, Pearl Meyer produced and reviewed market non-employee director compensation data, participated in certain compensation committee meetings and prepared an assessment of and recommendations with respect to our non-employee director compensation. In February 2019, the committee assessed the independence of Pearl Meyer and concluded that no conflict of interest exists that would prevent Pearl Meyer from providing the services performed for the compensation committee under such engagement. In November 2020, the compensation committee engaged Pearl Meyer as an independent compensation consultant to assess the market competitiveness of our executive compensation and provide the compensation committee with recommendations based on such assessment. At the compensation committee's request, Pearl Meyer produced and reviewed market executive compensation data, participated in certain compensation committee meetings and prepared an assessment of and recommendations with respect to our executive compensation. In November 2020, the committee assessed the independence of Pearl Meyer and concluded that no conflict of interest exists that would prevent Pearl Meyer from providing the services performed for the compensation committee under such engagement. The compensation committee did not engage any other consultants with respect to 2019, 2020 or 2021 compensation matters.

We received a favorable advisory vote on the compensation of our named executive officers at our 2021 annual meeting of stockholders, with over 83% of the votes cast with respect to such matter voting in favor of such compensation. The compensation committee believes those voting results affirm our stockholders' support of our approach to executive compensation and did not make any material changes to its approach. The compensation committee will continue to consider the outcome of our advisory votes to approve executive compensation when making future decisions with respect to the compensation paid to our named executive officers.

Corporate and Individual Performance Criteria

February 2019 Compensation Determinations

In February 2019, the compensation committee made determinations regarding 2018 cash bonus awards and 2019 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2018:

- our efforts in support of applications for regulatory approval filed by Sanofi to market sotagliflozin for type 1 diabetes in the United States and the European Union and the acceptance of such applications by the United States Food and Drug Administration and the European Medicines Agency;
- our progress relative to our objectives in preparing for the commercial launch of sotagliflozin in the United States for the treatment of type 1 diabetes;
- our progress relative to our objectives for the commercial performance of and medical support for XERMELO (telotristat ethyl) in the United States;
- our progress relative to our objectives in advancing the clinical development of telotristat ethyl in biliary tract cancer;
- our progress relative to our objectives in advancing our other clinical and preclinical drug development programs; and
- our performance relative to our objectives for financial performance and business development, specifically relating to year-end cash and investments and management of our financial resources.

The committee's compensation determinations in February 2019 reflected its assessment that we largely achieved our objectives relating to sotagliflozin, partially achieved our objectives relating to XERMELO and largely achieved our objectives relating to our other drug development programs and our financial performance. Taking into account the balance of factors described above, it was the committee's assessment that our overall corporate objectives were partially achieved.

For named executive officers other than Mr. Coats, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each named executive officer towards the achievement of the year's corporate goals, together with Mr. Coats' and the committee's independent assessment of each named executive officer's overall performance and contributions to the company during the year, in the course of making subjective judgments about individual performance in connection with compensation determinations. Mr. Coats had no individual goals for 2018 apart from the corporate goals.

The committee's determinations for Mr. Coats were based entirely upon its determination of achievement of the year's corporate goals, together with the compensation committee's assessment of his strategic and operational leadership. For other named executive officers, the compensation committee based its determinations principally upon its determination of achievement of the year's corporate goals, but also took into account, to a lesser extent, each named executive officer's individual goals. In the case of Mr. Wade, the compensation committee took into account his contributions toward our financial management, the successful operation of our commercial financial systems and our other business development and alliance management activities, as well as his strategic and operational leadership. In the case of Mr. Crum, the compensation committee took into account his contributions toward our legal and compliance oversight, as well as his strategic and operational leadership. In the case of Dr. Main, the compensation committee took into account his contributions toward our commercial supply of XERMELO and clinical and preclinical supply of our development programs, as well as his strategic and operational leadership.

February 2020 Compensation Determinations

In February 2020, the compensation committee made determinations regarding 2019 cash bonus awards and 2020 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2019:

- the regulatory approval to market sotagliflozin for type 1 diabetes in the European Union;
- our efforts in support of the application for regulatory approval to market sotagliflozin for type 1 diabetes in the United States and the dispute resolution process relating to such application;
- our efforts in support of the transfer of the sotagliflozin program from Sanofi following the termination of our alliance with Sanofi for the development and commercialization of sotagliflozin;

- our progress relative to our objectives for the commercial performance of and medical support for XERMELo in the United States;
- our progress relative to our objectives in advancing the clinical development of telotristat ethyl in biliary tract cancer;
- our progress relative to our objectives in advancing the clinical development of LX9211 in neuropathic pain;
- our progress relative to our objectives in advancing our other clinical and preclinical drug development programs; and
- our performance relative to our objectives for financial performance and business development, specifically relating to year-end cash and investments and management of our financial resources.

The committee's compensation determinations in February 2020 reflected its assessment that we largely achieved our objectives relating to sotagliflozin, XERMELo (telotristat ethyl), our other drug development programs and our financial performance. Taking into account the balance of factors described above, it was the committee's assessment that our overall corporate objectives were largely achieved.

For named executive officers other than Mr. Coats, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each named executive officer towards the achievement of the year's corporate goals, together with Mr. Coats' and the committee's independent assessment of each named executive officer's overall performance and contributions to the company during the year, in the course of making subjective judgments about individual performance in connection with compensation determinations. Mr. Coats had no individual goals for 2019 apart from the corporate goals.

The committee's determinations for Mr. Coats were based entirely upon its determination of achievement of the year's corporate goals, together with the compensation committee's assessment of his strategic and operational leadership. For other named executive officers, the compensation committee based its determinations principally upon its determination of achievement of the year's corporate goals, but also took into account, to a lesser extent, each named executive officer's individual goals. In the case of Mr. Wade, the compensation committee took into account his contributions toward our financial management, the successful operation of our commercial financial systems and our other business development and alliance management activities, as well as his strategic and operational leadership. In the case of Mr. Crum, the compensation committee took into account his contributions toward our legal and compliance oversight, as well as his strategic and operational leadership. In the case of Dr. Main, the compensation committee took into account his contributions toward our commercial supply of XERMELo and clinical and preclinical supply of our development programs, as well as his strategic and operational leadership.

February 2021 Compensation Determinations

In February 2021, the compensation committee made determinations regarding 2020 cash bonus awards and 2021 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2020:

- our progress relative to our objectives for the commercial performance of and medical support for XERMELo in the United States;
- our progress relative to our objectives in advancing the clinical development of telotristat ethyl in biliary tract cancer;
- our completion of the sale of XERMELo and related assets to TerSera Therapeutics LLC;
- our efforts to strategically refocus the company on sotagliflozin, LX9211 and our other clinical and preclinical stage programs following the sale of XERMELo and restructure the company in alignment with such renewed strategic focus;
- our efforts in support of the transfer of the sotagliflozin program from Sanofi following the termination of our alliance with Sanofi for the development and commercialization of sotagliflozin;
- our announcement of positive results from two Phase 3 clinical trials evaluating sotagliflozin's effect on cardiovascular deaths, hospitalizations for heart failure and urgent heart failure visits, and the publication of data from such studies in the *New England Journal of Medicine*;
- our progress relative to our objectives in advancing the clinical development of LX9211 in neuropathic pain;
- our progress relative to our objectives in advancing our other clinical and preclinical drug development programs; and

- our performance relative to our objectives for financial performance and business development, specifically relating to our debt reduction and capital raising efforts, year-end cash and investments and management of our financial resources.

The committee's compensation determinations in February 2021 reflected its assessment that we largely achieved our objectives relating to XERMELO (telotristat ethyl), sotagliflozin, LX9211, our other drug development programs and our financial performance. Taking into account the balance of factors described above, it was the committee's assessment that our overall corporate objectives were largely achieved.

For named executive officers other than Mr. Coats, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each named executive officer towards the achievement of the year's corporate goals, together with Mr. Coats' and the committee's independent assessment of each named executive officer's overall performance and contributions to the company during the year, in the course of making subjective judgments about individual performance in connection with compensation determinations. Mr. Coats had no individual goals for 2020 apart from the corporate goals.

The committee's determinations for Mr. Coats were based entirely upon its determination of achievement of the year's corporate goals, together with the compensation committee's assessment of his strategic and operational leadership. For other named executive officers, the compensation committee based its determinations principally upon its determination of achievement of the year's corporate goals, but also took into account, to a lesser extent, each named executive officer's individual goals. In the case of Mr. Wade, the compensation committee took into account his contributions toward our financial management, our debt reduction and capital raising efforts, the successful operation of our commercial financial systems and our business development and alliance management activities, as well as his strategic and operational leadership. In the case of Mr. Crum, the compensation committee took into account his contributions toward our legal and compliance oversight and our debt reduction and capital raising efforts, as well as his strategic and operational leadership. In the case of Dr. Main, the compensation committee took into account his contributions toward our commercial supply of XERMELO and clinical and preclinical supply of our development programs, as well as his strategic and operational leadership.

February 2022 Compensation Determinations

In February 2022, the compensation committee made determinations regarding 2021 cash bonus awards and 2022 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2021:

- our submission of a new drug application for sotagliflozin for the treatment of heart failure with the United States Food and Drug Administration;
- our progress in preparing for the commercial launch of sotagliflozin for the treatment of heart failure in the United States;
- our progress relative to our objectives in advancing the clinical development of LX9211 in neuropathic pain;
- our progress relative to our objectives in advancing our other clinical and preclinical drug development programs; and
- our performance relative to our objectives for financial performance and business development, specifically relating to our year-end cash and investments and management of our financial resources.

The committee's compensation determinations in February 2022 reflected its assessment that we significantly achieved our objectives relating to sotagliflozin, LX9211, our other drug development programs and our financial performance. Taking into account the balance of factors described above, it was the committee's assessment that our overall corporate objectives were significantly achieved.

For named executive officers other than Mr. Coats, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each named executive officer towards the achievement of the year's corporate goals, together with Mr. Coats' and the committee's independent assessment of each named executive officer's overall performance and contributions to the company during the year, in the course of making subjective judgments about individual performance in connection with compensation determinations. Mr. Coats had no individual goals for 2021 apart from the corporate goals.

The committee's determinations for Mr. Coats were based entirely upon its determination of achievement of the year's corporate goals, together with the compensation committee's assessment of his strategic and operational leadership. For other named executive officers, the compensation committee based its determinations principally upon its determination of achievement of the year's corporate goals, but also took into account, to a lesser extent, each named executive officer's

individual goals. In the case of Mr. Wade, the compensation committee took into account his contributions toward our financial management, our capital raising efforts, the successful operation of our financial systems and our business development and alliance management activities, as well as his strategic and operational leadership. In the case of Mr. Crum, the compensation committee took into account his contributions toward our legal and compliance oversight and our capital raising efforts, as well as his strategic and operational leadership. In the case of Dr. Granowitz, the compensation committee took into account his contributions toward the medical support of sotagliflozin and our other drug development programs, as well as his strategic and operational leadership. In the case of Dr. Main, the compensation committee took into account his contributions toward the clinical and preclinical supply of our development programs, as well as his strategic and operational leadership.

Compensation Elements

Base Salary

Base salary of executive and other officers is established through negotiation between the company and the officer at the time he or she is hired, and then subsequently adjusted when the officer's base compensation is subject to review or reconsideration. While we have entered into employment agreements with certain of our executive officers, these agreements provide that base salaries after the initial year will be reviewed and determined by the compensation committee. When establishing base salary levels for executive and other officers, the compensation committee, in accordance with its general compensation policy, considers numerous factors, including the responsibilities relating to the position, the qualifications of the executive and the relevant experience the individual brings to the company, strategic goals for which the executive has responsibility, and compensation levels of companies at a comparable stage of commercialization and development who compete with us for business, scientific and executive talents. When considering increases to base salary levels for officers, which typically occurs each February, we consider corporate and individual performance in addition to the foregoing factors. No pre-determined weights are given to any one of these factors.

In February 2019, 2020, 2021 and 2022, we increased base salaries for each of our named executive officers following reviews of peer group salary data. The base salaries of our named executive officers are generally competitive with those paid by our peer group companies, with most falling near the median for such peer group companies. In establishing base salaries for 2019, 2020, 2021 and 2022, we considered the competitiveness of our cash compensation arrangements for executive officers and our cash position and needs for the applicable year.

Cash Bonus Awards

In addition to base salary, we may award variable annual cash bonus awards to executive and other officers with reference to certain predefined corporate and personal performance goals. These performance goals include those discussed generally above, as well as strategic and operational goals for the company as a whole. We typically consider the award of cash bonuses each February relating to performance for the preceding year. For each of our officers, the compensation committee establishes a bonus target, expressed as a percentage of base salary, which is used to determine the cash bonus amount, assuming that corporate and individual goals are fully achieved. The compensation committee retains broad discretion over the amount and payment of such awards and is not bound by any pre-determined agreement, formula or other standard with respect to such decisions.

In determining the cash bonus awards paid in February 2020 with respect to 2019 performance, the compensation committee included the relevant factors described above under “- Corporate and Individual Performance Criteria - February 2020 Compensation Determinations” in its evaluation of corporate and individual performance. After taking into account these factors, the compensation committee determined that our objectives for the year had been largely achieved, and awarded bonuses for 2019 performance to our named executive officers in amounts reflecting such level of achievement.

In determining the cash bonus awards paid in February 2021 with respect to 2020 performance, the compensation committee included the relevant factors described above under “- Corporate and Individual Performance Criteria - February 2021 Compensation Determinations” in its evaluation of corporate and individual performance. After taking into account these factors, the compensation committee determined that our objectives for the year had been largely achieved, and awarded bonuses for 2020 performance to our named executive officers in amounts reflecting such level of achievement.

In determining the cash bonus awards paid in February 2022 with respect to 2021 performance, the compensation committee included the relevant factors described above under “- Corporate and Individual Performance Criteria - February 2022 Compensation Determinations” in its evaluation of corporate and individual performance. After taking into account these factors, the compensation committee determined that our objectives for the year had been significantly achieved, and awarded bonuses for 2021 performance to our named executive officers in amounts reflecting such level of achievement.

Long-Term Stock-Based Incentive Awards

All of our employees, including our named executive officers, are eligible to receive long-term stock-based incentive awards under our 2017 Equity Incentive Plan as a means of providing such individuals with a continuing proprietary interest in our success. These grants are typically awarded each February and align the interests of our employees and our stockholders by providing significant incentives for our employees to achieve and maintain high levels of performance. Our 2017 Equity Incentive Plan enhances our ability to attract and retain the services of qualified individuals. Factors considered in determining whether, in what form and in what amounts such awards are granted to an employee include the employee's position, his or her performance and responsibilities, the amount of stock options, restricted stock units and other stock awards currently held by the employee, the vesting schedules of any such stock options, restricted stock units and stock awards and the employee's other compensation. While we do not adhere to any firmly established formulas or schedules for the issuance of long-term stock-based incentive awards, we take into account, in making award decisions, the total direct compensation objectives described above. In addition, we will generally tailor the terms of any such grant to achieve its goal as a long-term incentive award by providing for a vesting schedule encompassing several years.

In February 2019, 2020, 2021 and 2022, the compensation committee approved a mix of annual stock option grants and restricted stock unit awards under our 2017 Equity Incentive Plan to eligible employees, with stock options comprising a larger portion of such mix for executive and other officers. In making such grants, the compensation committee considered corporate and individual performance in the prior year, total direct compensation objectives for individual officers, and information regarding stock incentive award grants made by other companies in the biopharmaceutical industry.

Summary Compensation Table for 2021

The following table presents summary information regarding the compensation of each of Lonnel Coats, our principal executive officer, Jeffrey L. Wade, our principal financial officer, and our three other most highly compensated executive officers who were serving as executive officers as of December 31, 2021. We have entered into employment arrangements with certain of our named executive officers, the material terms of each of which are described below.

Based on the summary compensation information provided below, "Salary" accounted for approximately 23.8%, 23.9% and 23.8% of the total compensation paid to our named executive officers in 2021, 2020 and 2019, respectively, and "Bonus" accounted for approximately 11.2%, 11.7% and 11.7% of the total compensation paid to our named executive officers for 2021, 2020 and 2019, respectively.

Name and Position	Year	Salary	Bonus	Stock Awards ⁽¹⁾	Option Awards ⁽²⁾	All Other Compensation ⁽³⁾	Total
Lonnel Coats	2021	\$ 688,825	\$ 438,645	\$ 838,000	\$ 1,946,000	\$ 12,620	\$ 3,924,090
Chief Executive Officer	2020	\$ 668,620	\$ 473,188	\$ 840,376	\$ 1,866,067	\$ 12,420	\$ 3,860,671
and Director	2019	\$ 649,196	\$ 459,406	\$ 1,228,802	\$ 1,520,667	\$ 12,220	\$ 3,870,291
Jeffrey L. Wade	2021	\$ 476,319	\$ 227,250	\$ 280,981	\$ 652,559	\$ 14,574	\$ 1,651,683
President and Chief	2020	\$ 456,372	\$ 184,967	\$ 302,534	\$ 671,790	\$ 13,839	\$ 1,629,502
Financial Officer	2019	\$ 444,431	\$ 181,817	\$ 491,488	\$ 484,471	\$ 12,116	\$ 1,614,323
Brian T. Crum	2021	\$ 407,609	\$ 135,450	\$ 219,975	\$ 510,890	\$ 14,429	\$ 1,288,353
Senior Vice President and	2020	\$ 387,747	\$ 136,986	\$ 208,828	\$ 463,687	\$ 12,192	\$ 1,209,201
General Counsel	2019	\$ 369,287	\$ 133,072	\$ 246,825	\$ 171,746	\$ 11,955	\$ 932,885
Craig B. Granowitz, M.D., Ph.D.	2021	\$ 188,322	\$ 73,175	\$ —	\$ 686,405	\$ 646	\$ 948,548
Senior Vice President and							
Chief Medical Officer							
Alan J. Main, Ph.D.	2021	\$ 414,024	\$ 148,016	\$ 225,673	\$ 523,993	\$ 12,158	\$ 1,323,864
Executive Vice President,	2020	\$ 403,824	\$ 144,406	\$ 231,369	\$ 513,765	\$ 11,945	\$ 1,305,309
Innovation and Chemical	2019	\$ 393,270	\$ 140,542	\$ 421,336	\$ 428,562	\$ 11,730	\$ 1,395,440
Sciences							

⁽¹⁾ Reflects the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of stock awards granted in 2021, 2020 and 2019, in each case based on the market price of our common stock on the date of grant, calculated in accordance with the process for determination of fair market value under our 2017 Equity Incentive Plan.

⁽²⁾ Reflects the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of stock options granted in 2021, 2020 and 2019. See the information appearing under the heading entitled "Stock-Based Compensation" in footnote 2 to our consolidated financial statements included as part of our Annual Report on Form 10-K for the year ended December 31, 2021 for certain assumptions made in the valuation of such stock options.

⁽³⁾ Includes the following amounts in respect of company matching contributions under our 401(k) plan and company-paid premiums for group term life insurance. The company-paid life insurance premiums reflect payments for group term life policies maintained for the benefit of

	Year		Company 401(k) Matching Contribution	Company Health Savings Account Matching Contribution	Company-Paid Group Term Life Insurance Premiums
Lonnell Coats	2021	\$	11,600 \$	— \$	1,020
	2020	\$	11,400 \$	— \$	1,020
	2019	\$	11,200 \$	— \$	1,020
Jeffrey L. Wade	2021	\$	11,600 \$	2,000 \$	974
	2020	\$	11,400 \$	1,500 \$	939
	2019	\$	11,200 \$	— \$	916
Brian T. Crum	2021	\$	11,600 \$	2,000 \$	829
	2020	\$	11,400 \$	— \$	792
	2019	\$	11,200 \$	— \$	755
Craig B. Granowitz, M.D., Ph.D.	2021	\$	— \$	333 \$	313
Alan J. Main, Ph.D.	2021	\$	11,600 \$	— \$	558
	2020	\$	11,400 \$	— \$	545
	2019	\$	11,200 \$	— \$	530
all employees.					

Employment Arrangements

Lonnell Coats. In July 2014, we entered into an offer letter with Lonnell Coats to serve as our president and chief executive officer. Mr. Coats has served as chief executive officer since October 2021. Under the offer letter, Mr. Coats receives a base salary, currently \$717,150 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The compensation committee has established a current bonus target for Mr. Coats of 70% of his base salary, subject to adjustment. The offer letter provides for certain severance payments upon the termination of Mr. Coats' employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

Jeffrey L. Wade. In December 1998, we entered into an employment agreement with Jeffrey L. Wade to serve as our senior vice president and chief financial officer starting in January 1999. Mr. Wade has served as president and chief financial officer since October 2021. Under the agreement, Mr. Wade receives a base salary, currently \$520,150 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The compensation committee has established a current bonus target for Mr. Wade of 50% of his base salary, subject to adjustment. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides for certain severance payments upon the termination of Mr. Wade's employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

Brian T. Crum. In November 2001, we entered into an offer letter with Brian T. Crum to serve as our senior corporate counsel. Mr. Crum has served as senior vice president and general counsel since October 2021. Under the offer letter, Mr. Crum receives a base salary, currently \$442,900, a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The compensation committee has established a current bonus target for Mr. Crum of 35% of his base salary, subject to adjustment.

Craig B. Granowitz, M.D., Ph.D. In July 2021, we entered into an offer letter with Craig B. Granowitz, M.D., Ph.D., to serve as our senior vice president and chief medical officer. Under the offer letter, Dr. Granowitz receives a base salary, currently \$473,800 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The compensation committee has established a current bonus target for Dr. Granowitz of 40% of his base salary, subject to adjustment. The offer letter provides for certain severance payments upon the termination of Dr. Granowitz's employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

Alan J. Main, Ph.D. In July 2001, we entered into an employment agreement with Alan J. Main, Ph.D., to serve as our senior vice president, Lexicon Pharmaceuticals. Dr. Main has served as executive vice president, innovation and chemical sciences since September 2020. Under the agreement, Dr. Main receives a base salary, currently \$435,591 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The compensation committee has established a current bonus target for Dr. Main of 35% of his base salary, subject

to adjustment. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides for certain severance payments upon the termination of Dr. Main's employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

Pay Ratio

As required by Section 953(b) of the Dodd-Frank Wall Street Reform and Consumer Protection Act, we are providing the following information regarding the annual total compensation of our chief executive officer and our employees:

- As disclosed in the Summary Compensation Table above, the annual total compensation of Lonnel Coats, our chief executive officer, was \$3,924,090 in 2021; and
- The annual total compensation of the employee identified as the median compensated employee of our company (other than Mr. Coats) was \$234,672 in 2021.

Based on this information, the ratio of the annual total compensation of Mr. Coats to the median of the annual total compensation of all employees was 17 to 1.

We identified our median compensated employee using our total employee population as of December 31, 2021 and consistently applying payroll records reflecting taxable wages for 2021. In making this identification, we annualized the compensation of all permanent employees who were newly hired during 2021. We did not use any material estimates, assumptions, adjustments or statistical sampling to identify our median compensated employee. Once identified, we calculated the annual total compensation of our median compensated employee in a manner consistent with that used to calculate the annual total compensation of Mr. Coats and disclosed in the Summary Compensation Table above.

SEC rules for identifying the median compensated employee and calculating the pay ratio based on that employee's annual total compensation allow companies to adopt a variety of methodologies, apply certain exclusions and make reasonable estimates and assumptions that reflect their compensation practices. As such, the pay ratio reported by other companies may not be comparable to the pay ratio reported above, as other companies may have different employment and compensation practices and may utilize different methodologies, exclusions, estimates and assumptions in calculating their pay ratios.

Grants of Plan-Based Awards in 2021

The following table presents each grant of restricted stock units and stock options in 2021 to the individuals named in the summary compensation table.

Name	Grant Date	Number of Restricted Stock Units	Number of Securities Underlying Options	Exercise Price of Option Awards	Grant Date Fair Value of Stock and Option Awards
Lonnel Coats	2/11/2021	100,000			\$ 838,000
	2/11/2021		300,000	\$ 8.38	\$ 1,946,000
Jeffrey L. Wade	2/11/2021	33,530			\$ 280,981
	2/11/2021		100,600	\$ 8.38	\$ 652,559
Brian T. Crum	2/11/2021	26,250			\$ 219,975
	2/11/2021		78,760	\$ 8.38	\$ 510,890
Craig B. Granowitz, M.D., Ph.D.	8/2/2021		250,000	\$ 3.54	\$ 686,405
Alan J. Main, Ph.D.	2/11/2021	26,930			\$ 225,673
	2/11/2021		80,780	\$ 8.38	\$ 523,993

Each of the restricted stock units in the foregoing table was granted under our 2017 Equity Incentive Plan. Each restricted stock unit granted to our named executive officers on February 11, 2021 vested with respect to one third of the shares underlying the restricted stock unit on February 28, 2022 and will vest with respect to an additional one third of the shares underlying the restricted stock unit on February 28 of each of the two following years. Each restricted stock unit becomes fully vested upon the termination of the named executive officer's employment by us without cause or by the named executive officer for good reason, in either case following a change in control of our company.

Each of the stock options in the foregoing table was granted under our 2017 Equity Incentive Plan and expires on the tenth anniversary of the grant date. Each option vests with respect to 25% of the shares underlying the option on the first anniversary of the grant date and 1/48th per month for each month of service thereafter. Each option becomes fully vested with respect to all remaining unvested shares upon a change in control of our company. In accordance with the process for determination of fair market value under the plan, the exercise price for each stock option is equal to the closing price of our

common stock, as quoted on the Nasdaq Global Select Market, on the last trading day prior to the grant date. The exercise price for each stock option may be paid in cash or in shares of our common stock valued at fair market value on the exercise date or through a cashless exercise procedure involving a same-day sale of the purchased shares.

Outstanding Equity Awards at December 31, 2021

The following table presents information about unexercised stock options and unvested restricted stock units that were held by each of the individuals listed in the summary compensation table as of December 31, 2021.

	Option Awards				Stock Awards	
	Number of Securities Underlying Unexercised Options		Option Exercise Price	Option Expiration Date	Number of Restricted Stock Units That Have Not Vested ^(a)	Market Value of Restricted Stock Units That Have Not Vested ^(a)
	Exercisable	Unexercisable ^(b)				
Lonnell Coats	121,928	—	\$ 11.76	7/7/2024		
	173,371	—	\$ 6.23	2/5/2025		
	134,230	—	\$ 8.20	2/11/2026		
	85,780	—	\$ 14.44	2/9/2027		
	202,794	8,816	\$ 9.79	2/8/2028		
	313,274	128,986	\$ 5.16	2/7/2029		
	349,096	412,564	\$ 3.31	2/6/2030		
	—	300,000	\$ 8.38	2/11/2031		
					79,380	\$ 312,757
					169,260	\$ 666,884
				100,000	\$ 394,000	
Jeffrey L. Wade	44,570	—	\$ 12.60	2/15/2022		
	38,856	—	\$ 14.63	2/8/2023		
	46,856	—	\$ 12.04	2/6/2024		
	92,914	—	\$ 6.23	2/5/2025		
	71,940	—	\$ 8.20	2/11/2026		
	44,770	—	\$ 14.44	2/9/2027		
	76,238	3,312	\$ 9.79	2/8/2028		
	99,810	41,090	\$ 5.16	2/7/2029		
	125,681	148,519	\$ 3.31	2/6/2030		
	—	100,600	\$ 8.38	2/11/2031		
				25,290	\$ 99,643	
				60,933	\$ 240,076	
				33,530	\$ 132,108	
Brian T. Crum	10,571	—	\$ 12.60	2/15/2022		
	8,747	—	\$ 14.63	2/8/2023		
	13,499	—	\$ 12.04	2/6/2024		
	19,391	—	\$ 6.23	2/5/2025		
	23,470	—	\$ 8.20	2/11/2026		
	14,160	—	\$ 14.44	2/9/2027		
	22,082	958	\$ 9.79	2/8/2028		
	35,390	14,560	\$ 5.16	2/7/2029		
	86,746	102,514	\$ 3.31	2/6/2030		
	—	78,760	\$ 8.38	2/11/2031		
				11,100	\$ 43,734	
				42,060	\$ 165,716	
				26,250	\$ 103,425	
Craig B. Granowitz, M.D., Ph.D.	—	250,000	\$ 3.54	8/2/2031		

	Option Awards				Stock Awards	
	Number of Securities Underlying Unexercised Options		Option Exercise Price	Option Expiration Date	Number of Restricted Stock Units That Have Not Vested ⁽²⁾	Market Value of Restricted Stock Units That Have Not Vested ⁽³⁾
	Exercisable	Unexercisable ⁽¹⁾				
Alan J. Main, Ph.D.	39,999	—	\$ 12.60	2/15/2022		
	37,713	—	\$ 14.63	2/8/2023		
	42,856	—	\$ 12.04	2/6/2024		
	84,342	—	\$ 6.23	2/5/2025		
	65,340	—	\$ 8.20	2/11/2026		
	39,960	—	\$ 14.44	2/9/2027		
	67,028	2,912	\$ 9.79	2/8/2028		
	88,295	36,345	\$ 5.16	2/7/2029		
	96,116	113,584	\$ 3.31	2/6/2030		
	—	80,780	\$ 8.38	2/11/2031		
					22,373	\$ 88,150
					46,600	\$ 183,604
					26,930	\$ 106,104

⁽¹⁾ Each stock option vests with respect to 25% of the shares underlying the stock option on the first anniversary of the grant date and 1/48th per month for each month of service thereafter.

⁽²⁾ Each restricted stock unit vests with respect to one third of the shares underlying the restricted stock unit on February 28 of each of the three years following the year of grant.

⁽³⁾ Based on the closing price of our common stock on the Nasdaq Global Select Market of \$3.94 per share on December 31, 2021.

Option Exercises and Stock Vested in 2021

The following table presents information about stock option exercises and the vesting of restricted stock units in 2021 for each of the individuals listed in the summary compensation table. Amounts shown under the columns “Value Realized on Exercise” and “Value Realized on Vesting” are based on the market price of our common stock on the date of exercise or vesting, as applicable, calculated in accordance with the process for determination of fair market value under our 2017 Equity Incentive Plan, without taking into account any taxes that may be payable in connection with the exercise or vesting event, subsequent sale of shares or any shares retained by us in satisfaction of any withholding obligations relating to such taxes.

Name	Option Awards		Stock Awards	
	Number of Shares Acquired on Exercise	Value Realized on Exercise	Number of Shares Acquired on Vesting	Value Realized on Vesting ⁽¹⁾
Lyonel Coats	—	\$ —	192,885	\$ 1,386,843
Jeffrey L. Wade	—	\$ —	68,109	\$ 489,704
Brian T. Crum	—	\$ —	38,765	\$ 278,720
Craig B. Granowitz, M.D., Ph.D.	—	\$ —	—	\$ —
Alan J. Main, Ph.D.	—	\$ —	56,468	\$ 406,005

⁽¹⁾ Based on the closing price of our common stock on the Nasdaq Global Select Market of \$7.19 per share on February 26, 2021, the last trading day prior to the date of vesting.

Potential Payments upon Termination or Change in Control

Offer Letters

Lyonel Coats. Our offer letter with Mr. Coats provides that if we terminate his employment without “cause,” we would pay Mr. Coats his then-current salary for twelve months pursuant to our normal payroll procedures. If such termination is in connection with a “change in control,” we will pay Mr. Coats an additional one-time payment equal to his bonus target for the year of termination.

Craig B. Granowitz, M.D., Ph.D. Our offer letter with Dr. Granowitz provides that if we terminate his employment without “cause,” we would pay Dr. Granowitz his then-current salary for six months pursuant to our normal payroll procedures. Such payments would be extended to twelve months if Dr. Granowitz’s employment were terminated without “cause” in connection with a “change in control.”

Under each of our offer letters with Mr. Coats and Dr. Granowitz, “cause” means any of the following:

- the individual having engaged in intentional misconduct causing our material violation of any state or federal laws;
- the individual having engaged in a theft of corporate funds or corporate assets or in a material act of fraud upon us;
- an act of personal dishonesty taken by the individual that was intended to result in personal enrichment of the individual at our expense; or
- the individual’s conviction of a felony.

Under each of our offer letters with Mr. Coats and Dr. Granowitz, a “change in control” shall have occurred upon any of the following events:

- any person becomes the beneficial owner of securities representing 50% or more of the combined voting power of our outstanding voting securities;
- the approval by our stockholders of a reorganization, merger, or consolidation pursuant to which our stockholders immediately prior to such reorganization, merger or consolidation do not, immediately thereafter, own or control more than 50% of the combined voting power of the surviving entity’s outstanding voting securities in substantially the same proportions as prior to such reorganization, merger or consolidation; or
- our liquidation or dissolution or the sale of all or substantially all of our assets.

Under our offer letters with Mr. Coats and Dr. Granowitz, a “change in control” shall not occur solely as a result of the majority ownership of our outstanding voting securities by Invus, L.P. or any future reduction in the percentage of our outstanding voting securities owned by Invus, L.P. below a majority level.

Employment Agreements

Jeffrey L. Wade. Our employment agreement with Mr. Wade provides that if we terminate his employment without “cause” or if Mr. Wade terminates his employment for “good reason,” we will pay Mr. Wade his then-current salary for twelve months pursuant to our normal payroll procedures, plus an additional single sum payment equal to 50% of his target bonus for the year in which the termination occurred, provided that if such termination occurs within 120 days following a reduction in his salary, the salary continuation payments shall be based on Mr. Wade’s salary prior to such reduction. If his employment is terminated at the end of any renewal term through notice of non-renewal, we will pay Mr. Wade his then-current salary for six months pursuant to our normal payroll procedures.

Alan J. Main. Our employment agreement with Dr. Main provides that if we terminate his employment without “cause” or if Dr. Main terminates his employment for “good reason,” we will pay Dr. Main his then-current salary for twelve months pursuant to our normal payroll procedures, plus an additional single sum payment equal to 50% of his target bonus for the year in which the termination occurred. If his employment is terminated at the end of any renewal term through notice of non-renewal, we will pay Dr. Main his then-current salary for six months pursuant to our normal payroll procedures.

Under each of our employment agreements with Mr. Wade and Dr. Main, “cause” means any of the following:

- the individual having engaged in intentional misconduct causing our material violation of any state or federal laws;
- the individual having engaged in a theft of corporate funds or corporate assets or in a material act of fraud upon us;
- an act of personal dishonesty taken by the individual that was intended to result in his personal enrichment at our expense;
- the individual’s final conviction in a court of competent jurisdiction of a felony; or

- a breach by the individual during his employment of the conflict of interest, confidential information and non-competition covenants under the agreement, if such breach results in a material injury to our company.

Under each of our employment agreements with Mr. Wade and Dr. Main, “good reason” means any of the following, without the individual’s prior written consent:

- any material diminution in the individual’s base compensation, followed by the individual terminating his employment for “good reason” within 120 days after receiving notice of such diminution;
- any material diminution in the individual’s authority, duties or responsibilities, followed by the individual terminating his employment for “good reason” within 120 days after receiving notice of such diminution; or
- any material breach by our company of the agreement, followed by the individual terminating his employment for “good reason” within 120 days after receiving notice of such breach.

Stock Option Agreements

Our stock option agreements with the individuals named in the summary compensation table provide that all remaining unvested stock options shall become fully vested upon a change in control of our company. Under the stock option agreements, a “change in control” shall have occurred upon any of the following events:

- any person other than Invus, L.P. and its affiliates becomes the beneficial owner of securities representing 35% or more of the combined voting power of our outstanding voting securities;
- the approval by our stockholders of a reorganization, merger, or consolidation pursuant to which our stockholders immediately prior to such reorganization, merger or consolidation do not, immediately thereafter, own or control more than 50% of the combined voting power of the surviving entity’s outstanding voting securities in substantially the same proportions as prior to such reorganization, merger or consolidation;
- our liquidation or dissolution or the sale of all or substantially all of our assets;
- the election by our stockholders of any person to our board of directors who has not been nominated for election by a majority of the board of directors or any duly appointed committee thereof;
- following the election or removal of directors, a majority of the board of directors consists of individuals who were not members of the board of directors two years before such election or removal, unless the election of such individuals to the board of directors has been approved in advance by directors representing a majority of the directors then in office who were directors at the beginning of the two-year period; or
- any other corporate event affecting the company deemed to be a “change in control” by the compensation committee.

Under the stock option agreements, a change in control shall also have occurred if Invus, L.P. and its affiliates become the beneficial owner of securities representing 50% or more of the combined voting power of our outstanding voting securities other than as a result of the consummation of any of the transactions contemplated by our securities purchase agreement and stockholders’ agreement with Invus, L.P. The pro rata rights offering to our stockholders which we completed in December 2011 and which resulted in Invus and its affiliates becoming the beneficial owner of more than 50% of the outstanding shares of our common stock did not constitute a change in control under the stock option agreements as it was contemplated by our securities purchase agreement with Invus, L.P.

Restricted Stock Unit Agreements

Our restricted stock unit agreements with the individuals named in the summary compensation table provide that the interest of each named executive officer in the shares subject to the restricted stock unit shall become fully vested upon the termination of the named executive officer’s employment by us without cause or by the named executive officer for good reason, in either case following a change in control of our company, or as a result of the named executive officer’s death or disability. Under the restricted stock unit agreements, a “change in control” shall have occurred upon any of the following events:

- any person other than Invus, L.P. and its affiliates becomes the beneficial owner of securities representing 35% or more of the combined voting power of our outstanding voting securities;

- the consummation of a reorganization, merger, or consolidation pursuant to which our stockholders immediately prior to such reorganization, merger or consolidation do not, immediately thereafter, own or control more than 50% of the combined voting power of the surviving entity's outstanding voting securities in substantially the same proportions as prior to such reorganization, merger or consolidation;
- our liquidation or dissolution or the sale of all or substantially all of our assets;
- following the election or removal of directors, a majority of the board of directors consists of individuals who were not members of the board of directors two years before such election or removal, unless the election of such individuals to the board of directors has been approved in advance by directors representing a majority of the directors then in office who were directors at the beginning of the two-year period; or
- any other corporate event affecting the company deemed to be a "change in control" by the compensation committee.

Under the restricted stock unit agreements, a change in control shall also have occurred if Invus, L.P. and its affiliates become the beneficial owner of securities representing 50% or more of the combined voting power of our outstanding voting securities other than as a result of the consummation of any of the transactions contemplated by our securities purchase agreement and stockholders' agreement with Invus, L.P. The pro rata rights offering to our stockholders which we completed in December 2011 and which resulted in Invus and its affiliates becoming the beneficial owner of more than 50% of the outstanding shares of our common stock did not constitute a change in control under the restricted stock unit agreements as it was contemplated by our securities purchase agreement with Invus, L.P.

Under the restricted stock unit agreements, "cause" means any of the following:

- the individual having engaged in intentional misconduct causing our material violation of any state or federal laws;
- the individual having engaged in a theft of corporate funds or corporate assets or in a material act of fraud upon us;
- an act of personal dishonesty taken by the individual that was intended to result in personal enrichment of the individual at our expense;
- the individual's final conviction, or entry of any plea other than "not guilty," in a court of competent jurisdiction of a felony; or
- a breach by the individual of any contractual or fiduciary obligation to us, if such breach results in a material injury to us.

Under the restricted stock unit agreements, "good reason" means any of the following, without the individual's prior written consent:

- any material diminution in the individual's base salary;
- any material diminution in the individual's authority, duties or responsibilities; or
- any material breach by our company of any contractual obligation to the individual.

The following table reflects the amounts the individuals named in the summary compensation table would have been entitled to receive if the foregoing termination or change-in-control events had occurred on December 31, 2021. The table does not take into account any taxes that may have been payable in connection with any of those payments:

Name	Aggregate Salary Continuation	Bonus	Other Compensation	Accelerated Portion of Stock Options ⁽⁵⁾	Accelerated Portion of Restricted Stock Units ⁽⁶⁾
Coats Lommel	\$ 696,262 ⁽¹⁾	\$ 487,383 ⁽¹⁾	\$ —	\$ 259,915	\$ 1,373,64
L. Wade Jeffrey	\$ 505,000 ⁽²⁾	\$ 126,250 ⁽²⁾	\$ —	\$ 93,567	\$ 471,82
T. Crum Brian	\$ —	\$ —	\$ —	\$ 64,584	\$ 312,87
B. Granowitz, M.D., Ph.D. Craig	\$ 460,000 ⁽³⁾	\$ —	\$ —	\$ 100,000	\$ —
Main, Ph.D. Alan J.	\$ 422,904 ⁽⁴⁾	\$ 74,008 ⁽⁴⁾	\$ —	\$ 71,558	\$ 377,85

- (1) Reflects aggregate salary continuation payments due as a result of our termination of Mr. Coats' employment without "cause" and bonus payments due as a result of our termination of Mr. Coats' employment without "cause" in connection with a "change in control."
- (2) Reflects aggregate salary continuation and partial bonus payments due as a result of our termination of Mr. Wade's employment without "cause" or Mr. Wade's termination of his employment for "good reason." If Mr. Wade's employment had been terminated at the end of a renewal term through notice of non-renewal, the aggregate salary continuation payment for Mr. Wade would have been \$252,500.
- (3) Reflects aggregate salary continuation payments due as a result of our termination of Dr. Granowitz's employment without "cause" in connection with a "change in control." If Dr. Granowitz's employment had been terminated without "cause" other than in connection with a "change in control," the aggregate salary continuation payment for Dr. Granowitz would have been \$230,000.
- (4) Reflects aggregate salary continuation and partial bonus payments due as a result of our termination of Dr. Main's employment without "cause" or Dr. Main's termination of his employment for "good reason." If Dr. Main's employment had been terminated at the end of a renewal term through notice of non-renewal, the aggregate salary continuation payment for Dr. Main would have been \$211,452.
- (5) Reflects the value associated with accelerated vesting of stock options upon the occurrence of a "change of control," and based on the closing price of our common stock on the Nasdaq Global Select Market on December 31, 2021 of \$3.94 per share, less the exercise price payable with respect to the stock options for which vesting would have been accelerated.
- (6) Reflects the value associated with accelerated vesting of restricted stock units upon termination of employment without "cause" or for "good reason," in each case following a "change of control," and based on the closing price of our common stock on the Nasdaq Global Select Market on December 31, 2021 of \$3.94 per share.

Director Compensation in 2021

Each non-employee member of our board of directors currently receives the following cash compensation:

- an annual retainer of \$45,000 for service on the board of directors (\$75,000 for service as non-executive chairman of the board of directors), prorated for any partial year of service;
- an annual retainer of \$10,000 for service on the audit committee of the board of directors (\$20,000 for service as chair of the audit committee), prorated for any partial year of service;
- an annual retainer of \$7,500 for service on the compensation committee of the board of directors (\$15,000 for service as chair of the compensation committee), prorated for any partial year of service; and
- an annual retainer of \$5,000 for service on the corporate governance committee of the board of directors (\$10,000 for service as chair of the corporate governance committee), prorated for any partial year of service.

Lyonel Coats, our chief executive officer, does not receive additional compensation for his service as a director.

Non-employee directors may also be granted stock options, restricted stock awards or restricted stock unit awards under our 2017 Non-Employee Directors' Equity Incentive Plan. Our board of directors determines the provision of each award granted under the plan, including the type of award, the number of shares subject to such award and any relevant vesting schedule. In accordance with the process for determination of fair market value under the plan, the exercise price for each stock option granted under the plan is equal to the closing price of our common stock, as quoted on the Nasdaq Global Select Market, on the last trading day prior to the grant date. Non-employee directors may not be granted awards under the plan with an aggregate grant date fair value of more than \$500,000 during any calendar year, taken together with the cash fees paid to such non-employee director in compensation for service on our board of directors during such calendar year.

The following table presents summary information for the year ended December 31, 2021 regarding the compensation of the non-employee members of our board of directors.

Name	Fees Earned or Paid in Cash		Option Awards ⁽¹⁾⁽²⁾⁽³⁾		Restricted Stock Unit Awards ⁽¹⁾⁽³⁾		All Other Compensation	Total
Raymond Debbane	\$	85,000	\$	25,340	\$	20,281	—	\$ 130,621
Phillippe J. Amouyal	\$	52,500	\$	25,340	\$	20,281	—	\$ 98,121
Samuel L. Barker, Ph.D.	\$	72,500	\$	25,340	\$	20,281	—	\$ 118,121
Robert J. Lefkowitz, M.D.	\$	50,000	\$	25,340	\$	20,281	—	\$ 95,621
Alan S. Nies, M.D.	\$	45,000	\$	25,340	\$	20,281	—	\$ 90,621
Frank P. Palantoni	\$	70,000	\$	25,340	\$	20,281	—	\$ 115,621
Christopher J. Sobacki	\$	45,000	\$	25,340	\$	20,281	—	\$ 90,621
Judith L. Swain, M.D.	\$	60,000	\$	25,340	\$	20,281	—	\$ 105,621

(1) Reflects the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of stock options and restricted stock awards granted in 2021. See the information appearing under the heading entitled "Stock-Based Compensation" in footnote 2 to our consolidated financial

statements included as part of our Annual Report on Form 10-K for the year ended December 31, 2021 for certain assumptions made in the valuation of such stock options and restricted stock awards.

Name	Number of Securities Underlying Unexercised Options
Raymond Debbane	51,108
Philippe J. Amouyal	51,108
Samuel L. Barker, Ph.D.	51,108
Robert J. Lefkowitz, M.D.	51,108
Alan S. Nies, M.D.	51,108
Frank P. Palantoni	51,108
Christopher J. Sobeci	51,108
Judith L. Swain, M.D.	51,108

(2) The non-employee members of our board of directors held the following aggregate number of unexercised options as of such date:

(3) The following table presents the fair value of each grant of stock options in 2021 to non-employee members of our board of directors, computed in accordance with FASB ASC Topic 718:

Name	Grant Date	Number of Securities Underlying Options	Exercise Price of Option Awards	Closing Market Price on the Grant Date of Option Awards	Grant Date Fair Value of Options
Raymond Debbane	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Philippe Amouyal	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Samuel L. Barker, Ph.D.	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Robert J. Lefkowitz, M.D.	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Alan S. Nies, M.D.	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Frank P. Palantoni	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Christopher J. Sobeci	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340
Judith L. Swain, M.D.	4/30/2021	6,475	\$ 5.04	\$ 4.86	25,340

(4) The following table presents the fair value of each grant of restricted stock unit awards in 2021 to non-employee members of our board of directors, computed in accordance with FASB ASC Topic 718:

Name	Grant Date	Number of Restricted Stock Unit Awards	Per Share Grant Date Fair Value	Grant Date Fair Value of Restricted Stock Unit Awards
Raymond Debbane	4/30/2021	4,024	\$ 5.04	20,281
Philippe Amouyal	4/30/2021	4,024	\$ 5.04	20,281
Samuel L. Barker, Ph.D.	4/30/2021	4,024	\$ 5.04	20,281
Robert J. Lefkowitz, M.D.	4/30/2021	4,024	\$ 5.04	20,281
Alan S. Nies, M.D.	4/30/2021	4,024	\$ 5.04	20,281
Frank P. Palantoni	4/30/2021	4,024	\$ 5.04	20,281
Christopher J. Sobeci	4/30/2021	4,024	\$ 5.04	20,281
Judith L. Swain, M.D.	4/30/2021	4,024	\$ 5.04	20,281

Compensation Committee Report

The compensation committee of our board of directors has been established to oversee the compensation of our employees, including our chief executive officer and other officers. The compensation committee also has responsibility for the evaluation and approval of all compensation plans, policies and programs, including the issuance of stock options, restricted stock units and other awards under our 2017 Equity Incentive Plan.

In performing these functions, the compensation committee has reviewed and discussed with the management of our company the information set forth above under the heading "Executive and Director Compensation - Compensation Discussion and Analysis." Based upon that review and discussion, the compensation committee has recommended to the board of directors that the information set forth above under the heading "Executive and Director Compensation - Compensation Discussion and Analysis" be included in this proxy statement and incorporated by reference into our annual report on Form 10-K for the year ended December 31, 2021.

Compensation Committee

Frank P. Palantoni (chair)
Philippe J. Amouyal
Samuel L. Barker, Ph.D.

The foregoing compensation committee report shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference by any general statement incorporating by reference this proxy statement into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate this compensation committee report by reference.

PROPOSALS OF STOCKHOLDERS

In order for a stockholder proposal to be considered for inclusion in our proxy statement for next year's annual meeting, we must receive the written proposal at our principal executive offices no later than December 9, 2022. Any such proposal must also comply with the procedures in Rule 14a-8 under the Securities and Exchange Act of 1934. Similarly, in order for any stockholder proposal to be otherwise raised during next year's annual meeting, we must receive written notice of the proposal, containing the information required by our bylaws, at our principal executive offices no later than December 9, 2022. You may contact our corporate secretary at our principal executive offices for a copy of the relevant bylaw provisions for making stockholder proposals.

FINANCIAL INFORMATION

Our annual report to stockholders, including financial statements, accompanies this proxy statement but does not constitute a part of the proxy solicitation materials. **You may obtain, without charge, a copy of our annual report on Form 10-K, including the financial statements and exhibits thereto, by written request to Corporate Communications, Lexicon Pharmaceuticals, Inc., 2445 Technology Forest Blvd., 11th Floor, The Woodlands, Texas 77381.**

By order of the board of directors,

/s/ Brian T. Crum

Brian T. Crum
Secretary

April 8, 2022
The Woodlands, Texas

**THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
LEXICON PHARMACEUTICALS, INC.**

LEXICON PHARMACEUTICALS, INC. (the "Corporation"), a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware ("DGCL"), hereby certifies as follows pursuant to Sections 242 and 245 of the DGCL:

FIRST: The name of the Corporation is "Lexicon Pharmaceuticals, Inc." The Corporation was previously incorporated as "Lexicon Genetics Incorporated."

SECOND: The original Certificate of Incorporation of the Corporation was filed in the Office of the Secretary of State of the State of Delaware (the "Secretary of State") on July 7, 1995. An Amended and Restated Certificate of Incorporation of the Corporation was filed in the Office of the Secretary of State on April 26, 2012 and was subsequently amended by a Certificate of Amendment to the Amended and Restated Certificate of Incorporation filed in the Office of the Secretary of State on May 20, 2015. A Second Amended and Restated Certificate of Incorporation of the Corporation was filed in the Office of the Secretary of State on April 30, 2021.

THIRD: The Board of Directors of the Corporation (the "Board of Directors"), in accordance with Sections 242 and 245 of the DGCL, (i) adopted and approved this Third Amended and Restated Certificate of Incorporation (including the amendments to the Corporation's Certificate of Incorporation effected hereby) and (ii) proposed that the Corporation's stockholders adopt and approve this Third Amended and Restated Certificate of Incorporation (including the amendments to the Corporation's Certificate of Incorporation effected hereby).

FOURTH: The holders of not less than a majority of the outstanding shares of the Corporation's common stock, par value \$.001 per share, and preferred stock, par value \$0.01 per share, in accordance with Sections 242 and 245 of the DGCL, approved and adopted on behalf of the stockholders this Third Amended and Restated Certificate of Incorporation (including the amendments to the Corporation's Certificate of Incorporation effected hereby).

FIFTH: This Third Amended and Restated Certificate of Incorporation shall become effective on its filing with the Secretary of State.

SIXTH: The Second Amended and Restated Certificate of Incorporation of the Corporation is hereby amended and restated to read in its entirety as follows:

ARTICLE I

Name

The name of the Corporation is "Lexicon Pharmaceuticals, Inc."

ARTICLE II

Registered Office and Registered Agent

The registered office of the Corporation in the State of Delaware is located at Corporation Trust Center, 1209 Orange Street in the City of Wilmington, County of New Castle. The name of the registered agent of the Corporation at such address is The Corporation Trust Company.

ARTICLE III

Purpose

The purpose for which the Corporation is organized is to engage in any lawful acts and activities for which corporations may be organized under the General Corporation Law of the State of Delaware ("DGCL").

ARTICLE IV

Capitalization

Section 4.01 Authorized Capital. (a) The total number of shares of stock that the Corporation shall have the authority to issue is 305,000,000 shares of capital stock, consisting of (i) 5,000,000 shares of preferred stock, par value \$0.01

per share (the “Preferred Stock”), and (ii) 300,000,000 shares of common stock, par value \$0.001 per share (the “Common Stock”).

(b) Subject to the provisions of this Certificate of Incorporation and the Preferred Stock Designation (as defined below) creating any series of Preferred Stock, the Corporation may issue shares of its capital stock from time to time for such consideration (not less than the par value thereof) as may be fixed by the Board of Directors of the Corporation (the “Board of Directors”), which is expressly authorized to fix the same in its absolute discretion subject to the foregoing conditions. Shares so issued for which the consideration shall have been paid or delivered to the Corporation shall be deemed fully paid stock and shall not be liable to any further call or assessment thereon, and the holders of such shares shall not be liable for any further payments in respect of such shares.

(c) The right to cumulate votes for the election of directors as provided in Section 214 of the DGCL shall not be granted and is hereby expressly denied.

(d) Subject to Article XII, no stockholder of the Corporation shall by reason of his or her holding shares of any class of capital stock of the Corporation have any preemptive or preferential right to acquire or subscribe for any additional, unissued or treasury shares (whether now or hereafter acquired) of any class of capital stock of the Corporation now or hereafter to be authorized, or any notes, debentures, bonds or other securities convertible into or carrying any right, option or warrant to subscribe for or acquire shares of any class of capital stock of the Corporation now or hereafter to be authorized, whether or not the issuance of any such shares or such notes, debentures, bonds or other securities would adversely affect the dividends or voting or other rights of that stockholder.

Section 4.02 Preferred Stock. (a) The Preferred Stock may be issued from time to time in one or more series. Authority is hereby expressly granted to and vested in the Board of Directors to authorize from time to time the issuance of Preferred Stock in one or more series. With respect to each series of Preferred Stock authorized by it, the Board of Directors shall be authorized to establish by resolution or resolutions, and by filing a certificate pursuant to applicable law of the State of Delaware (the “Preferred Stock Designation”), the following to the fullest extent now or hereafter permitted by the DGCL:

- (1) the designation of such series;
- (2) the number of shares to constitute such series;
- (3) whether such series is to have voting rights (full, special or limited) or is to be without voting rights;

(4) if such series is to have voting rights, whether or not such series is to be entitled to vote as a separate class either alone or together with the holders of the Common Stock or one or more other series of Preferred Stock;

(5) the preferences and relative, participating, optional, conversion or other special rights (if any) of such series and the qualifications, limitations or restrictions (if any) with respect to such series;

(6) the redemption rights and price(s), if any, of such series, and whether or not the shares of such series shall be subject to the operation of retirement or sinking funds to be applied to the purchase or redemption of such shares for retirement and, if such retirement or sinking funds or funds are to be established, the periodic amount thereof and the terms and provisions relative to the operation thereof;

(7) the dividend rights and preferences (if any) of such series, including, without limitation, (i) the rates of dividends payable thereon, (ii) the conditions upon which and the time when such dividends are payable, (iii) whether or not such dividends shall be cumulative or noncumulative and, if cumulative, the date or dates from which such dividends shall accumulate and (iv) whether or not the payment of such dividends shall be preferred to the payment of dividends payable on the Common Stock or any other series of Preferred Stock;

(8) the preferences (if any), and the amounts thereof, which the holders of such series shall be entitled to receive upon the voluntary or involuntary liquidation, dissolution or winding-up of, or upon any distribution of the assets of, the Corporation;

(9) whether or not the shares of such series, at the option of the Corporation or the holders thereof or upon the happening of any specified event, shall be convertible into or exchangeable for (i) shares of Common Stock, (ii) shares of any other series of Preferred Stock or (iii) any other stock or securities of the Corporation;

(10) if such series is to be convertible or exchangeable, the price or prices or ratio or ratios or rate or rates at which such conversion or exchange may be made and the terms and conditions (if any) upon which such price or prices or ratio or ratios or rate or rates may be adjusted; and

(11) such other rights, powers and preferences with respect to such series as may to the Board of Directors seem advisable.

Any series of Preferred Stock may vary from any other series of Preferred Stock in any or all of the foregoing respects and in any other manner.

(b) The Board of Directors may, with respect to any existing series of Preferred Stock but subject to the Preferred Stock Designation creating such series, (i) increase the number of shares of Preferred Stock designated for such series by a resolution adding to such series authorized and unissued shares of Preferred Stock not designated for any other series and (ii) decrease the number of shares of Preferred Stock designated for such series by a resolution subtracting from such series shares of Preferred Stock designated for such series (but not below the number of shares of such series then outstanding), and the shares so subtracted shall become authorized, unissued and undesignated shares of Preferred Stock.

(c) No vote of the holders of the Common Stock or the Preferred Stock shall, unless otherwise expressly provided in a Preferred Stock Designation creating any series of Preferred Stock, be a prerequisite to the issuance of any shares of any series of the Preferred Stock authorized by and complying with the conditions of this Certificate of Incorporation. Shares of any series of Preferred Stock that have been authorized for issuance pursuant to this Certificate of Incorporation and that have been issued and reacquired in any manner by the Corporation (including upon conversion or exchange thereof) shall be restored to the status of authorized and unissued shares of Preferred Stock and may be reissued as part of a new series of Preferred Stock to be created by resolution or resolutions of the Board of Directors and a Preferred Stock Designation as set forth above.

Section 4.03. Common Stock. (a) The holders of shares of the Common Stock shall be entitled to vote upon all matters submitted to a vote of the common stockholders of the Corporation and shall be entitled to one vote for each share of the Common Stock held.

(b) Subject to the prior rights and preferences (if any) applicable to shares of Preferred Stock of any series, the holders of shares of the Common Stock shall be entitled to receive such dividends (payable in cash, stock or otherwise) as may be declared thereon by the Board of Directors at any time and from time to time out of any funds of the Corporation legally available therefor.

(c) In the event of any voluntary or involuntary liquidation, dissolution or winding-up of the Corporation, after payment or provision for payment of the debts and other liabilities of the Corporation and subject to the preferential or other rights (if any) of the holders of shares of the Preferred Stock in respect thereof, the holders of shares of the Common Stock shall be entitled to receive all the remaining assets of the Corporation available for distribution to its stockholders, ratably in proportion to the number of shares of the Common Stock held by them. For purposes of this paragraph (c), a liquidation, dissolution or winding-up of the Corporation shall not be deemed to be occasioned by or to include (i) any consolidation or merger of the Corporation with or into another corporation or other entity or (ii) a sale, lease, exchange or conveyance of all or a part of the assets of the Corporation.

Section 4.04. Stock Options, Warrants, etc. Unless otherwise expressly prohibited in the Preferred Stock Designation creating any series of Preferred Stock, the Corporation shall have authority to create and issue warrants, rights and options entitling the holders thereof to purchase from the Corporation shares of the Corporation's capital stock of any class or series or other securities of the Corporation for such consideration and to such persons, firms or corporations as the Board of Directors, in its sole discretion, may determine, setting aside from the authorized but unissued capital stock of the Corporation the requisite number of shares for issuance upon the exercise of such warrants, rights or options. Such warrants, rights and options shall be evidenced by one or more instruments approved by the Board of Directors. The Board of Directors shall be empowered to set the exercise price, duration, time for exercise and other terms of such warrants, rights or options; *provided, however*, that the consideration to be received for any shares of capital stock subject thereto shall not be less than the par value thereof.

ARTICLE V
Directors

Section 5.01. Number and Term. The number of directors of the Corporation shall from time to time be fixed exclusively by the Board of Directors in accordance with, and subject to the limitations set forth in, the bylaws of the Corporation (the "Bylaws"); *provided, however*, that the Board of Directors shall at all times consist of a minimum of three and a maximum of 13 directors, subject, however, to increases above 13 directors as may be required in order to permit the holders of any series of Preferred Stock to exercise their right (if any) to elect additional directors under specified circumstances or to permit the election or appointment to the Board of Directors of the Required Director Number of Investor Designated Directors (each as defined in the Stockholders' Agreement, dated as of June 17, 2007, between Invus, L.P. and the Corporation (as amended, supplemented or otherwise modified, the "Stockholders' Agreement")) pursuant to the Stockholders' Agreement. No decrease in the number of directors shall have the effect of shortening the term of any incumbent director. Anything in this Certificate of Incorporation or the Bylaws to the contrary notwithstanding, each director shall hold office until his successor is elected and qualified or until his earlier death, resignation or removal.

Section 5.02. Limitation of Personal Liability. (a) No person who is or was a director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the Corporation or its stockholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under Section 174 of the DGCL or (iv) for any transaction from which the director derived an improper personal benefit.

(b) If the DGCL is hereafter amended to authorize corporate action further limiting or eliminating the personal liability of directors, then the personal liability of the directors to the Corporation or its stockholders shall be limited or eliminated to the fullest extent permitted by the DGCL, as so amended from time to time.

Section 5.03. Classification. The Board of Directors shall be divided into three classes designated as Class I, Class II and Class III, respectively, all as nearly equal in number as possible, with each director then in office receiving the classification to be determined with respect to such director by the Board of Directors. The initial term of office of Class I directors shall expire at the annual meeting of the Corporation's stockholders in 2001. The initial term of office of Class II directors shall expire at the annual meeting of stockholders in 2002. The initial term of office of Class III directors shall expire at the annual meeting of stockholders in 2003. Each director elected at an annual meeting of stockholders to succeed a director whose term is then expiring shall hold office until the third annual meeting of stockholders after his election or until his successor is elected and qualified or until his earlier death, resignation or removal. Increases and decreases in the number of directors shall be apportioned among the classes of directors so that all classes will be as nearly equal in number as possible. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

Section 5.04. Nomination and Election. (a) Nominations of persons for election or reelection to the Board of Directors may be made by or at the direction of the Board of Directors. The Bylaws may set forth procedures for the nomination of persons for election or reelection to the Board of Directors and only persons who are nominated in accordance with such procedures (if any) shall be eligible for election or reelection as directors of the Corporation; *provided, however*, that such procedures shall not infringe upon (i) the right of the Board of Directors to nominate persons for election or reelection to the Board of Directors or (ii) the rights of the holders of any class or series of Preferred Stock, voting separately by class or series, to elect additional directors under specified circumstances.

(b) Each director shall be elected in accordance with this Certificate of Incorporation, the Bylaws and applicable law. Election of directors by the Corporation's stockholders need not be by written ballot unless the Bylaws so provide.

Section 5.05. Removal. No director of any class may be removed before the expiration of his term of office except for cause and then only by the affirmative vote of the holders of not less than a majority in voting power of all the outstanding shares of capital stock of the Corporation entitled to vote generally in an election of directors, voting together as a single class. The Board of Directors may not remove any director, and no recommendation by the Board of Directors that a director be removed may be made to the Corporation's stockholders unless such recommendation is set forth in a resolution adopted by the affirmative vote of not less than 66-2/3% of the whole Board of Directors.

Section 5.06. Vacancies. (a) In case any vacancy shall occur on the Board of Directors because of death, resignation or removal, such vacancy may be filled only by a majority (or such higher percentage as may be specified in the Bylaws) of the directors remaining in office (though less than a quorum), or by the sole remaining director. The director so appointed shall serve for the unexpired term of his predecessor or until his successor is elected and qualified or until his earlier

death, resignation or removal. If there are no directors then in office, an election of directors may be held in the manner provided by applicable law.

(b) Any newly-created directorship resulting from any increase in the number of directors may be filled only by a majority (or such higher percentage as may be specified in the Bylaws) of the directors then in office (though less than a quorum), or by the sole remaining director. The director so appointed shall be assigned to such class of directors as such majority of directors or the sole remaining director, as the case may be, shall determine; *provided, however*, that newly-created directorships shall be apportioned among the classes of directors so that all classes will be as nearly equal in number as possible. Each director so appointed shall hold office for the remaining term of the class to which he is assigned or until his successor is elected and qualified or until his earlier death, resignation or removal.

(c) Except as expressly provided in this Certificate of Incorporation or as otherwise provided by applicable law, stockholders of the Corporation shall not have the right to fill vacancies on the Board of Directors, including newly-created directorships.

Section 5.07. Subject to Rights of Holders of Preferred Stock. Notwithstanding the foregoing provisions of this Article V, if the Preferred Stock Designation creating any series of Preferred Stock entitles the holders of such Preferred Stock, voting separately by class or series, to elect additional directors under specified circumstances, then all provisions of such Preferred Stock Designation relating to the nomination, election, term of office, removal, filling of vacancies and other features of such directorships shall, as to such directorships, govern and control over any conflicting provisions of this Article V, and such directors so elected need not be divided into classes pursuant to this Article V unless expressly provided by the provisions of such Preferred Stock Designation.

ARTICLE VI
Amendment of Bylaws

The Board of Directors is expressly authorized and empowered to adopt, alter, amend or repeal the Bylaws. Stockholders of the Corporation shall have the power to alter, amend, expand or repeal the Bylaws but only by the affirmative vote of the holders of not less than 66-2/3% in voting power of all outstanding shares of capital stock of the Corporation entitled to vote generally at an election of directors, voting together as a single class.

ARTICLE VII
Actions and Meetings of Stockholders

Section 7.01. No Action by Written Consent. No action shall be taken by the stockholders of the Corporation except at an annual or special meeting of stockholders. Stockholders of the Corporation may not act by written consent in lieu of a meeting.

Section 7.02. Meetings. (a) Meetings of the stockholders of the Corporation (whether annual or special) may only be called by the Board of Directors or by such officer or officers of the Corporation as the Board of Directors may from time to time authorize to call meetings of the stockholders of the Corporation. Stockholders of the Corporation shall not be entitled to call any meeting of stockholders or to require the Board of Directors or any officer or officers of the Corporation to call a meeting of stockholders except as otherwise expressly provided in the Bylaws or in the Preferred Stock Designation creating any series of Preferred Stock.

(b) Stockholders of the Corporation shall not be entitled to propose business for consideration at any meeting of stockholders except as otherwise expressly provided in the Bylaws or in the Preferred Stock Designation creating any series of Preferred Stock.

(c) Business transacted at any special meeting of stockholders shall be limited to the purposes stated in the notice or waivers of notice of such meeting. The person presiding at a meeting of stockholders may determine whether business has been properly brought before the meeting and, if the facts so warrant, such person may refuse to transact any business at such meeting which has not been properly brought before such meeting.

Section 7.03. Appoint and Remove Officers, etc. The stockholders of the Corporation shall have no right or power to appoint or remove officers of the Corporation nor to abrogate the power of the Board of Directors to elect and remove officers of the Corporation. The stockholders of the Corporation shall have no power to appoint or remove directors as members of committees of the Board of Directors nor to abrogate the power of the Board of Directors to establish one or more such committees or the power of any such committee to exercise the powers and authority of the Board of Directors.

Section 7.04. Compromises and Arrangements. Whenever a compromise or arrangement is proposed between this corporation and its creditors or any class of them and/or between this corporation and its stockholders or any class of them, any court of equitable jurisdiction within the State of Delaware may, on the application in a summary way of this corporation or of any creditor or stockholder thereof or on the application of any receiver or receivers appointed for this corporation under § 291 of Title 8 of the Delaware Code or on the application of trustees in dissolution or of any receiver or receivers appointed for this corporation under § 279 of Title 8 of the Delaware code order a meeting of the creditors or class of creditors, and/or of the stockholders or class of stockholders of this corporation, as the case may be, to be summoned in such manner as the said court directs. If a majority in number representing three fourths in value of the creditors or class of creditors, and/or of the stockholders or class of stockholders of this corporation, as the case may be, agree to any compromise or arrangement and to any reorganization of this corporation as a consequence of such compromise or arrangement, the said compromise or arrangement and the said reorganization shall, if sanctioned by the court to which the said application has been made, be binding on all the creditors or class of creditors, and/or on all the stockholders or class of stockholders, of this corporation, as the case may be, and also on this corporation.

ARTICLE VIII

Indemnification of Directors and Officers

The Corporation shall indemnify, to the fullest extent permitted by applicable law and pursuant to the Bylaws, each person who is or was a director or officer of the Corporation, and may indemnify each employee and agent of the Corporation and all other persons whom the Corporation is authorized to indemnify under the provisions of the DGCL.

ARTICLE IX

Election to be Governed by Section 203 of the DGCL

The Corporation hereby elects to be governed by Section 203 of the DGCL; *provided, however*, that the provisions of this Article IX shall not apply to restrict a business combination between the Corporation and an interested stockholder (as defined in Section 203 of the DGCL) of the Corporation if either (i) such business combination was approved by the Board of Directors prior to the time that such stockholder became an interested stockholder or (ii) such stockholder became an interested stockholder as a result of, and at or prior to the effective time of, a transaction which was approved by the Board of Directors prior to the time that such stockholder became an interested stockholder.

ARTICLE X

Amendment of Certificate of Incorporation

The Corporation reserves the right to amend, alter, change or repeal any provisions contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by applicable law, and all rights conferred upon stockholders, directors or any other persons by or pursuant to this Certificate of Incorporation are granted subject to this reservation. Notwithstanding the foregoing or any other provision of this Certificate of Incorporation or any provision of law that might otherwise permit a lesser or no vote, the provisions of this Article X and of Articles V, VI, VII and VIII may not be repealed or amended in any respect, and no provision inconsistent with any such provision or imposing cumulative voting in the election of directors may be added to this Certificate of Incorporation, unless such action is approved by the affirmative vote of the holders of not less than 66-2/3% in voting power of all outstanding shares of capital stock of the Corporation entitled to vote generally at an election of directors, voting together as a single class; *provided, however*, that any amendment or repeal of Section 5.02 or Article VIII of this Certificate of Incorporation shall not adversely affect any right or protection existing thereunder in respect of any act or omission occurring prior to such amendment or repeal and, *provided further*, that no Preferred Stock Designation shall be amended after the issuance of any shares of the Series of Preferred Stock created thereby, except in accordance with the terms of such Preferred Stock Designation and the requirements of applicable law.

ARTICLE XI

Voting Requirements Not Exclusive

The voting requirements contained in this Certificate of Incorporation shall be in addition to the voting requirements imposed by law or by the Preferred Stock Designation creating any series of Preferred Stock.

ARTICLE XII
Certain Rights of Covered Stockholders

Section 12.01. Rights to Purchase New Securities. (a) Notwithstanding Section 4.01(d), in the event that the Corporation proposes to issue New Securities, a Covered Stockholder shall have the right to purchase, in lieu of the person to whom the Corporation proposed to issue such New Securities, in accordance with paragraph (b) below, a number of New Securities equal to the product of (i) the total number or amount of New Securities which the Corporation proposes to issue at such time and (ii) a fraction, the numerator of which shall be the total number of shares of Common Stock which the Covered Stockholder beneficially owns at the relevant measurement point, and the denominator of which shall be the aggregate number of shares of Common Stock then outstanding (the number referred to in clause (ii), the "Pro Rata Share").

(b) Subject to the provisions of Section 12.01(c), in the event that the Corporation proposes to undertake an issuance of New Securities, it shall give written notice (a "Notice of Issuance") of its intention to the Covered Stockholder indicating the price per New Security (or, to the extent not reasonably known to the Corporation at such time, the methodology for determining such price) and the number of New Securities to be issued by the Corporation, and describing the material terms of the New Securities and the material terms upon which the Corporation proposes to issue such New Securities. The Covered Stockholder shall have two business days from the date of receipt of the Notice of Issuance to agree to purchase all or a portion of the Covered Stockholder's Pro Rata Share of such New Securities (as determined pursuant to paragraph (a) above) for the same consideration and otherwise upon the terms specified in the Notice of Issuance (unless better terms are provided to any other purchaser) by giving written notice to the Corporation and stating therein the quantity of New Securities to be purchased by the Covered Stockholder. If the Covered Stockholder exercises its right to purchase New Securities pursuant to this Section 12.01(b), the purchase and sale of such New Securities shall close at the same time as the issuance of New Securities to the other purchaser or purchasers and, subject to the preceding sentence, shall be issued on the same terms and subject to the same conditions as applicable to the other purchaser or purchasers; *provided that* (i) such terms and conditions applicable to the Covered Stockholder shall not include any restrictions on the transferability of such New Securities (except pursuant to applicable laws and regulations) or any standstill, voting or other restrictions, (ii) the Covered Stockholder shall not be required to make any representations and warranties except those that relate solely to the Covered Stockholder and (iii) the Covered Stockholder will not be required to undertake any indemnification obligation.

The rights given by the Corporation under this Section 12.01(b) shall terminate if unexercised within two business days after receipt of the Notice of Issuance referred to in this Section 12.01(b). Notwithstanding anything to the contrary contained herein, if (i) the price or any other material terms upon which the Corporation proposes to issue such New Securities are amended by the Corporation following the delivery to the Covered Stockholder of the Notice of Issuance or (ii) the offering of New Securities to which a Notice of Issuance relates is not completed within five business days from the delivery of such notice to the Covered Stockholder, the Covered Stockholder's election with respect to the purchase of New Securities covered by such Notice of Issuance shall be void and the Corporation shall be obligated to deliver a new Notice of Issuance to the Covered Stockholder, and the Covered Stockholder shall be entitled to make a new election with respect to the purchase by it of New Securities covered by such notice within the two-business day period from the date of delivery of the new Notice of Issuance and otherwise in accordance with the procedure specified in the second sentence of this Section 12.01(b).

(c) Notwithstanding anything to the contrary contained in Section 12.01(b), if the Corporation proposes to issue New Securities in an aggregate amount of at least \$25,000,000 in a Public Offering, the Notice of Issuance may, in lieu of specifying the price at which the Corporation proposes to issue New Securities and the number of New Securities to be issued by the Corporation in such offering, provide an estimated aggregate public offering size (in dollar amount) of the New Securities (exclusive of any Overallotment Securities, as contemplated by the following paragraph) that the Corporation estimates will ultimately be issued in such offering (the "Estimated Offering Size") and, to the extent different from the closing price per share of the Common Stock on the Nasdaq Stock Market or the principal securities exchange on which the Common Stock is then listed on the date immediately prior to the date on which the Notice of Issuance is delivered to the Covered Stockholder pursuant to this Section 12.01(c), an estimated public offering price per New Security (such closing price of the Common Stock or, if specified in such Issuance Notice, the estimated price per New Security so specified, the "Estimated Offering Price"). If the Covered Stockholder desires to exercise its rights under this Section 12.01 with respect to such Public Offering, the Covered Stockholder shall be required to make an election with respect to the purchase, at the public offering price in such Public Offering, of a dollar amount of New Securities up to its Pro Rata Share of the Estimated Offering Size no later than two business days from the date of receipt of the Notice of Issuance (which period shall be reduced to one business day if, prior to delivery of such Notice of Issuance, such Covered Stockholder, to the extent requested by the Corporation, had not entered into a customary agreement reasonably satisfactory to the Corporation requiring that the Covered Stockholder maintain the confidentiality of the proposed Public Offering unless and until publicly announced by the Corporation); *provided that* the Covered Stockholder's obligation to purchase the dollar amount of New Securities subject to its election shall be conditioned upon (i) the issuance by the Corporation of New Securities in such Public Offering at an aggregate public offering

price of at least 85% and no more than 115% of the Estimated Offering Size and (ii) the New Securities so issued being priced not higher than 15% above the Estimated Offering Price. For clarity, in the event the Covered Stockholder does not purchase the dollar amount of New Securities subject to its election in reliance upon the foregoing proviso, the Covered Stockholder shall be deemed to have chosen not to exercise its rights under this Section 12.01 with respect to such Public Offering.

Any Notice of Issuance provided by the Corporation to the Covered Stockholder in connection with a Public Offering may specify that the underwriters or agents in such offering shall be entitled to purchase upon exercise of an overallotment option, if any, additional New Securities in an amount up to 15% of the New Securities issued in such Public Offering (the "Overallotment Securities"). If the Covered Stockholder desires to exercise its rights under this Section 12.01 with respect to Overallotment Securities, the Covered Stockholder shall be required to make an election with respect to the purchase of up to its Pro Rata Share of the Overallotment Securities at the same time the Covered Stockholder makes an election pursuant to Section 12.01(c); *provided* that the Covered Stockholder's obligation to purchase Overallotment Securities in accordance with its election shall be subject to the same conditions to which its obligations to purchase New Securities in the Public Offering, before giving effect to such Overallotment Securities, are subject.

If a Public Offering contemplated by Section 12.01(c) is not completed within five business days following the Notice of Issuance with respect thereto, then the Corporation will be required to comply again with the provisions of this Section 12.01(c) in order to avail itself of the benefits of Section 12.01(c). In case a Public Offering contemplated by this Section 12.01(c) is consummated, the Covered Stockholder shall be obligated to purchase the New Securities which it has elected to purchase hereunder at the closing of such Public Offering if and to the extent the conditions to the Covered Stockholder's obligations hereunder are met, on the same terms and subject to the same conditions that would be applicable to the underwriters in such offering; *provided, however*, that (i) such terms and conditions applicable to the Covered Stockholder shall not include any restrictions on the transferability of such New Securities (except pursuant to applicable laws and regulations) or any standstill, voting or other restrictions, (ii) the Covered Stockholder shall not be required to make any representations and warranties except those that relate solely to the Covered Stockholder and (iii) the Covered Stockholder shall not be required to undertake any indemnity obligations.

Notwithstanding any other provision of this section, the Corporation may, in lieu of allowing the Covered Stockholder to participate in a Public Offering in fulfillment of its rights under this Section 12.01(c), offer instead to issue and sell to the Covered Stockholder up to a number of New Securities equal to the Covered Stockholder's Pro Rata Share of the New Securities issued in such Public Offering in a concurrent private placement on terms reasonably acceptable to both parties and at a price equal to the price at which the New Securities are sold to the public in the Public Offering.

Section 12.02. Approval of the Covered Stockholder Required for Certain Actions. In addition to any approval by the Board of Directors required by this Certificate of Incorporation, the Bylaws, applicable laws and regulations or Nasdaq Stock Market, the prior written approval of the Covered Stockholder shall be required in order for the Corporation to take, or the Board of Directors to approve, authorize or effect, any of the following (including by merger, consolidation or otherwise):

(a) the creation (by reclassification or otherwise) or issuance of any new class or series of shares of capital stock of the Corporation (or securities convertible into or exercisable for shares of capital stock of the Corporation) having rights, preferences or privileges senior to or on parity with the Common Stock;

(b) any action to repurchase, retire, redeem or otherwise acquire any equity securities (or securities convertible into or exchangeable for equity securities) of the Corporation or any subsidiary of the Corporation, pursuant to self-tender offers, stock repurchase programs, open market transactions, privately-negotiated purchases or similar transactions; *provided* that no consent of the Covered Stockholder pursuant to this section shall be required in connection with the repurchase, retirement, redemption or other acquisition by the Corporation of securities issued or issuable upon any exercise of options or vesting or exercise of any other equity-based award, in each case under the Corporation's equity incentive plans or any other plan or agreement approved by the Board of Directors, to pay the applicable exercise price or taxes associated with such awards;

(c) take any action to adopt, or propose to adopt, or maintain any shareholders' rights plan, "poison pill" or other similar plan or agreement, unless the Covered Stockholder is exempt from the provisions of such shareholders' rights plan, "poison pill" or other similar plan or agreement; or

(d) any authorization of, or entering into an agreement for, or the commitment to agree to take, any of the foregoing actions.

Section 12.03 **Definitions.** For purposes of this Article XII:

“Covered Stockholder” means a person that is the beneficial owner of 20% or more of the Corporation’s outstanding Common Stock as reflected in the person’s most recent filings under section 13 of the Securities Exchange Act of 1934, as amended, and that continues to be the beneficial owner of more than 20% of the Corporation’s Common Stock immediately prior to the time of the transaction or event to which the Covered Stockholder is entitled to rights under this Article XII; provided that for a person to be considered a “Covered Stockholder,” such person must send a written notice to the Corporation at its corporate offices, which notice must contain the number of shares of Common Stock beneficially owned by such person and the notice information, which must include a valid email address, at which such person may be reached for purposes of this Article XII.

“New Securities” means any capital stock of the Corporation, whether now authorized or not, and rights, options or warrants to purchase such capital stock, and securities of any type whatsoever (including convertible debt securities) that are, or may become, convertible into or exchangeable or exercisable for capital stock of the Corporation; *provided* that the term “New Securities” does not include (a) Common Stock or rights, options or warrants to acquire Common Stock of the Corporation issued to employees, consultants, officers or directors of the Corporation or any Subsidiary, or which have been reserved for issuance, pursuant to an employee stock option, stock purchase, stock bonus plan, or other similar compensation plan or arrangement approved by the Board of Directors, (b) securities of the Corporation issued to all then-existing stockholders in connection with any stock split, stock dividend, reclassification or recapitalization of the Corporation, (c) securities of the Corporation issued upon the conversion or exercise of exchangeable or convertible securities of the Corporation, including warrants and convertible notes, that are (i) outstanding as of the date of this Certificate of Incorporation of the Corporation or (ii) issued subsequently after receipt of the consent of the Covered Stockholder pursuant to Section 12.02, (d) securities of the Corporation issued as consideration in the acquisition of business or assets of another person, (e) Common Stock not otherwise contemplated by the foregoing clauses (a) through (d) issued in a given fiscal year pursuant to an “at the market” offering in an amount that does not exceed, in the aggregate, 2% of the outstanding Common Stock of the Corporation calculated as of the end of the preceding fiscal year, and (g) securities of the Corporation issued in connection with a transaction of the type described in Rule 145 under the Securities Act of 1933, as amended.

“Public Offering” means an underwritten public offering of New Securities that is registered under the Securities Act of 1933, as amended.

IN WITNESS WHEREOF, this Third Amended and Restated Certificate of Incorporation has been executed for and on behalf and in the name of the Corporation by its officers thereunto duly authorized on [], 2022.

LEXICON PHARMACEUTICALS, INC.

By: — Lonnel Coats
Chief Executive Officer

Attest:

By: — Brian T. Crum
Secretary

LEXICON PHARMACEUTICALS, INC.
 2445 TECHNOLOGY FOREST BLVD., 11th FLOOR
 THE WOODLANDS, TX 77381

VOTE BY INTERNET - www.proxyvote.com

Use the Internet to transmit your voting instructions and for electronic delivery of information. Vote by 11:59 P.M. ET on 05/19/2022. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

ELECTRONIC DELIVERY OF FUTURE PROXY MATERIALS

If you would like to reduce the costs incurred by our company in mailing proxy materials, you can consent to receiving all future proxy statements, proxy cards and annual reports electronically via e-mail or the Internet. To sign up for electronic delivery, please follow the instructions above to vote using the Internet and, when prompted, indicate that you agree to receive or access proxy materials electronically in future years.

VOTE BY PHONE - 1-800-690-6903

Use any touch-tone telephone to transmit your voting instructions. Vote by 11:59 P.M. ET on 05/19/2022. Have your proxy card in hand when you call and then follow the instructions.

VOTE BY MAIL

Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

x

KEEP THIS PORTION FOR YOUR RECORDS

DETACH AND RETURN THIS PORTION ONLY

THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED

	For All o	Withhold All o	For All Except o	To withhold authority to vote for any individual nominee(s), mark "For All Except" and write the number(s) of the nominee(s) on the line below
The Board of Directors recommends you vote FOR the following:				
1. Election of Directors				
Nominees				
01 Raymond Debbane		02 Robert J. Lefkowitz, MD		03 Alan S. Nies, MD
The Board of Directors recommends you vote FOR the following proposals.				
2. Ratification and approval of the Company's Third Amended and Restated Certificate of Incorporation	For o		Against o	Abstain o
3. Advisory vote to approve the compensation paid to the Company's named executive officers	For o		Against o	Abstain o
4. Ratification and approval of the appointment of Ernst & Young LLP as the Company's independent auditors for the fiscal year ending December 31, 2022	For o		Against o	Abstain o
Note: In their discretion, upon such other matters that may properly come before the meeting or any adjournment or adjournments thereof.				
Please sign exactly as your name(s) appear(s) hereon. When signing as attorney, executor, administrator, or other fiduciary, please give full title as such. Joint owners should each sign personally. All holders must sign. If a corporation or partnership, please sign in full corporate or partnership name, by authorized officer.				
Signature (PLEASE SIGN WITHIN BOX)		Date		Signature (Joint Owners)
				Date

Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting: The Notice & Proxy Statement, Annual Report is/are available at www.proxyvote.com.

Lexicon Pharmaceuticals, Inc.
Annual Meeting of Stockholders
May 20, 2022
This Proxy is solicited by the Board of Directors

The stockholder(s) hereby appoint(s) Lonnel Coats and Jeffrey L. Wade, or either of them, as proxies, each with the power to appoint his substitute, and hereby authorizes them to represent and to vote, as designated on the reverse side of this ballot, all of the shares of Common Stock of Lexicon Pharmaceuticals, Inc. that the stockholder(s) is/are entitled to vote at the Annual Meeting of Stockholders to be held at 8:00 a.m. CDT on May 20, 2022 online at <http://www.virtualshareholdermeeting.com/LRX2022>, and any adjournment or postponement thereof.

THIS PROXY, WHEN PROPERLY EXECUTED, WILL BE VOTED AS DIRECTED BY THE STOCKHOLDER(S). IF NO SUCH DIRECTIONS ARE MADE, THIS PROXY WILL BE VOTED FOR THE ELECTION OF THE NOMINEES LISTED ON THE REVERSE SIDE FOR THE BOARD OF DIRECTORS AND FOR EACH PROPOSAL.

Continued and to be signed on reverse side