

LEXICON PHARMACEUTICALS, INC./DE
Form PRE 14A
February 24, 2012
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 x
Filed by a Party other than the Registrant

Check the appropriate box:

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

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):

- x No fee required.
- o 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
- (5) Total fee paid: \$0
 - o Fee paid previously with preliminary materials: N/A
 - o 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.

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

(4) Date Filed

March ____, 2012

TO OUR STOCKHOLDERS:

I am pleased to invite you to attend the 2012 annual meeting of stockholders of Lexicon Pharmaceuticals, Inc. to be held on Thursday, April 26, 2012 at 8:00 a.m. CDT at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas.

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. Your proxy will not be used if you are present at the annual meeting and prefer to vote in person or if you revoke your proxy.

Thank you for your ongoing support of and continued interest in Lexicon Pharmaceuticals. We look forward to seeing you at the annual meeting.

Sincerely,

Arthur T. Sands, M.D., Ph.D.
President and Chief Executive Officer

LEXICON PHARMACEUTICALS, INC.

8800 Technology Forest Place

The Woodlands, Texas 77381

(281) 863-3000

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS

TO BE HELD APRIL 26, 2012

TO OUR STOCKHOLDERS:

The annual meeting of stockholders of Lexicon Pharmaceuticals, Inc. will be held on Thursday, April 26, 2012 at 8:00 a.m. CDT at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas, to:

elect three Class III directors;

ratify and approve an amended and restated certificate of incorporation (1) increasing the maximum number of members of our board of directors from twelve to 13 and (2) allowing for an increase above 13 directors as may be required for Invus, L.P. and Invus C.V. to exercise their rights to elect or appoint directors under our stockholders' agreement with Invus, L.P.;

ratify and approve an amendment to our Equity Incentive Plan (1) increasing the total number of shares of our common stock that may be issued pursuant to stock awards granted under the plan from 35,000,000 to 50,000,000 shares and (2) increasing the number of shares of our common stock that may be issued pursuant to awards other than stock options and stock appreciation rights from 3,500,000 to 15,000,000 shares;

ratify and approve an amendment to our Non-Employee Directors' Stock Option Plan (1) increasing the total number of shares of our common stock that may be issued pursuant to stock awards granted under the plan from 1,200,000 to 1,500,000 shares, (2) expanding the types of potential awards under the plan to include restricted stock awards, (3) replacing the annual option grant to purchase 10,000 shares of our common stock (or 20,000 shares in the case of the non-employee chairman of our board of directors) with an annual option grant to purchase 20,000 shares and an annual grant of restricted stock with a fair market value of \$20,000 and (4) renaming the plan the Non-Employee Directors' Equity Incentive Plan;

hold an advisory vote on the compensation paid to our named executive officers;

ratify and approve the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2012; and

act 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 February 29, 2012.

It is important that your shares be represented at the annual meeting whether or not you plan to attend. 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 are present at the annual meeting, and wish to do so, you may revoke the proxy and vote in person.

By order of the board of directors,

Brian T. Crum

Secretary

The Woodlands, Texas

March __, 2012

LEXICON PHARMACEUTICALS, INC.

8800 Technology Forest Place
The Woodlands, Texas 77381
(281) 863-3000

PROXY STATEMENT

FOR

ANNUAL MEETING OF STOCKHOLDERS

To Be Held April 26, 2012

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 2012 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, on or about March ___, 2012, 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 Thursday, April 26, 2012 at 8:00 a.m. CDT at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas.

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 three Class III directors;

• a proposal to ratify and approve an amended and restated certificate of incorporation (1) increasing the maximum number of members of our board of directors from twelve to 13 and (2) allowing for an increase above 13 directors as may be required for Invus, L.P. and Invus C.V. to exercise their rights to elect or appoint directors under our stockholders' agreement with Invus, L.P.;

• a proposal to ratify and approve an amendment to our Equity Incentive Plan (1) increasing the total number of shares of our common stock that may be issued pursuant to stock awards granted under the plan from 35,000,000 to 50,000,000 shares and (2) increasing the number of shares of our common stock that may be issued pursuant to awards other than stock options and stock appreciation rights from 3,500,000 to 15,000,000 shares;

• a proposal to ratify and approve an amendment to our Non-Employee Directors' Stock Option Plan (1) increasing the total number of shares of our common stock that may be issued pursuant to stock awards granted under the plan from 1,200,000 to 1,500,000 shares, (2) expanding the types of potential awards under the plan to include restricted stock awards, (3) replacing the annual option grant to purchase 10,000 shares of our common stock (or 20,000 shares in the case of the non-employee chairman of our board of directors) with an annual option grant to purchase 20,000 shares and an annual grant of restricted stock with a fair market value of \$20,000 and (4) renaming the plan the Non-Employee Directors' Equity Incentive Plan;

• an advisory vote on 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, 2012.

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 February 29, 2012, the record date for the annual meeting established by our board of directors. On the record date, _____ 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 or by proxy. 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 III 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 III 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 amended and restated certificate of incorporation will require the affirmative vote of 66 2/3% of the shares of our common stock outstanding on the record date. 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 ratification and approval of the amendments to our Equity Incentive Plan and Non-Employee Directors' Stock Option Plan, 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, 2012 will each require the affirmative vote of a majority of the votes cast with respect to such matters. Any abstention or broker non-vote with respect to such matters will not count as a vote for or against these proposals and will not be considered in calculating the number of votes necessary for their approval.

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 in person at the annual meeting 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 in person. Even if you vote by proxy, if you wish, you can revoke your proxy and vote in person 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 February 29, 2012 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.

2

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 III 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 amended and restated certificate of incorporation, the ratification and approval of the amendments to our Equity Incentive Plan and Non-Employee Directors' Stock Option Plan, 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, 2012, or abstain from voting on those proposals.

If any of our nominees for election as Class III 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 III 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 III directors and in favor of the ratification and approval of our amended and restated certificate of incorporation, the ratification and approval of the amendments to our Equity Incentive Plan and Non-Employee Directors' Stock Option Plan, 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, 2012.

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.
8800 Technology Forest Place
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 in person 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.

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 for inspection at 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 8800 Technology Forest Place, 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

3

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.

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 Shareowner Services LLC, and inform them of your request by calling them at (877) 854-4583 or writing them at 480 Washington Boulevard, Jersey City, New Jersey 07310.

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.

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 III directors will expire at this annual meeting. The current terms of our Class I and Class II directors will expire at our 2013 and 2014 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 III directors until our 2015 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 III Directors

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

| Name | Age | Position with the Company | Year First Became a Director |
|------------------------------|-----|--|------------------------------|
| Arthur T. Sands, M.D., Ph.D. | 50 | President and Chief Executive Officer and Director (Class III) | 1995 |
| Philippe J. Amouyal | 53 | Director (Class III) | 2007 |
| Frank P. Palantoni | 54 | Director (Class III) | 2004 |

Arthur T. Sands, M.D., Ph.D. co-founded our company and has been our president and chief executive officer and a director since September 1995. At Lexicon, Dr. Sands pioneered the development of large-scale gene knockout technology for use in drug discovery. Before founding Lexicon, Dr. Sands served as an American Cancer Society postdoctoral fellow in the Department of Human and Molecular Genetics at Baylor College of Medicine. He received his B.A. in economics and political science from Yale University and his M.D. and Ph.D. from Baylor College of Medicine.

Dr. Sands provides us with the benefit of his experience as an entrepreneur and founder of our company, as well as the institutional knowledge and organizational and management skills he has developed as our president and chief executive officer.

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 is a director of Weight Watchers International, Inc., as well as a number of private companies in which Invus has invested. He 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 Invus C.V. pursuant to our stockholders' agreement with Invus described under the heading “Transactions with Related Persons - Arrangements with Invus.”

Frank P. Palantoni has been a director since November 2004. Mr. Palantoni is president of the pet and animal health division of Central Garden & Pet Company. Previously, he was a partner at P3 Capital Management LLC, an early stage consumer products equity fund. Mr. Palantoni served as chief executive officer of Prestige Brands Holding, Inc. from April to June 2006 and as a director from January to June 2006. From 1998 to 2004, Mr. Palantoni held a variety of senior management positions with Novartis AG, most recently as president and chief executive officer, worldwide of its Gerber Products Company, Novartis Infant and Baby Division. Mr. Palantoni also served as president and chief executive officer for North American operations of Novartis Consumer Health Division from 2000 to 2001. Prior to

joining Novartis, he held a series of senior management positions with The Danone Group. He 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.

The Board of Directors recommends that stockholders vote "FOR" the foregoing nominees for election as Class III directors.

Current and Continuing Directors

The current directors of the Company are identified below:

| Name | Age | Position with the Company |
|--|-----|--|
| Arthur T. Sands, M.D., Ph.D. | 50 | President and Chief Executive Officer and Director (Class III) |
| Raymond Debbane ⁽³⁾ | 57 | Chairman of the Board of Directors (Class I) |
| Philippe J. Amouyal ⁽²⁾ | 53 | Director (Class III) |
| Samuel L. Barker, Ph.D. ^{(1) (2)} | 69 | Director (Class II) |
| Robert J. Lefkowitz, M.D. ⁽³⁾ | 68 | Director (Class I) |
| Alan S. Nies, M.D. ⁽²⁾ | 74 | Director (Class I) |
| Frank P. Palantoni ^{(1) (2)} | 54 | Director (Class III) |
| Christopher J. Sobecki | 53 | Director (Class II) |
| Judith L. Swain, M.D. ^{(1) (3)} | 63 | 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 Dr. Sands, Mr. Amouyal and Mr. Palantoni is set forth above under the heading “- Nominees for Class III Directors.”

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. In 1999, Artal became the controlling shareholder of Weight Watchers International, Inc., for which Mr. Debbane serves as chairman of the board of directors. He also serves as chairman or director of a number of private companies in which Invus and Artal Group S.A. have invested. 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 20 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 Invus C.V. 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 March 2005 to February 2012. In March 2001, Dr. Barker co-founded Clearview Projects, Inc., a provider of partnering and transaction services to biopharmaceutical companies, and served as its president and chief executive officer from July 2003 until November 2004. 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 during 1998; president, United States Pharmaceuticals from 1992 to 1997; and president, Bristol-Myers Squibb Intercontinental Commercial Operations from 1990 to 1992. Prior to 1990, Dr. Barker 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 Cadence Pharmaceuticals, Inc. and served as a director of AtheroGenics, Inc. from 2006 to 2009. 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.

Robert J. Lefkowitz, M.D. has been a director since February 2001 and a consultant to our company since March 2003. 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 Shaw Prize, the Albany Medical Center Prize and the 2007 National Medal of Science presented to him by President George W. Bush. 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 35 years as a member of the faculty at Duke University Medical Center.

Alan S. Nies, M.D. has been a director since November 2003 and chairman of our medical advisory board since March 2003. From 1992 through September 2002, Dr. Nies served in a series of senior management positions at Merck & Co. Inc., most recently as senior vice president, clinical sciences from 1999 to 2002. 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.

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 Weight Watchers International, Inc., as well as a number of private companies in which Invus has invested. Mr. Sobecki served as a director of NitroMed, Inc. from 2006 to 2009. 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 Invus C.V. 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 the executive director of the Singapore Institute for Clinical Sciences within A*STAR, and the Lien Chow Professor of Medicine at the National University of Singapore. From 2005 to 2006, she was the dean for translational medicine at the University of California, San Diego. Dr. Swain served as chair of the Department of Medicine at Stanford University from 1997 to 2005, and previously served on the medical faculties of the University of Pennsylvania and Duke University. Dr. Swain is currently a director of the Burroughs Wellcome Fund and a member of the Council of the Institute of Medicine, National Academies of Science. She has 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 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 AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

Our stockholders' agreement with Invus, L.P. provides that Invus, L.P. and Invus C.V., which we collectively refer to as Invus, have the right to designate a number of directors equal to the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, rounded up to the nearest whole number of directors. 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, to the extent permitted by applicable law and the rules and regulations of the Nasdaq Stock Market. Invus and its affiliates currently own approximately 58.3% of the outstanding shares of our common stock and have designated three of the nine current members of our board of directors.

Invus-designated directors currently serve as one of the four members of the compensation committee and one of the

three members of the corporate governance committee of our board of directors.

Invus' rights with respect to the designation of 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.

7

Although Invus has indicated that it does not have any current plans to designate additional directors or make additional appointments to the audit, compensation or corporate governance committees of our board of directors pursuant to these rights, we are asking that stockholders ratify and approve an amended and restated certificate of incorporation (1) increasing the maximum number of members of our board of directors from twelve to 13 and (2) allowing for an increase above 13 directors as may be required for Invus to exercise these rights, with the objective of enabling us to effect Invus' potential exercise of its rights under the stockholders' agreement in as expeditious and efficient manner as possible. The complete text of the amended and restated certificate of incorporation is set forth in Appendix A to this proxy statement.

You should be aware that, as a result of Invus' rights under the stockholders' agreement, our directors who were appointed by Invus may have interests in the amended and restated certificate of incorporation that are different from, or in addition to, their interests as stockholders generally. Our board of directors was aware of these interests and considered them, among other matters, in making its recommendation below.

The Board of Directors recommends that stockholders vote "FOR" the ratification and approval of the amended and restated certificate of incorporation.

PROPOSAL NUMBER 3:

RATIFICATION AND APPROVAL OF AMENDMENT TO EQUITY INCENTIVE PLAN

We use stock options and other stock awards as a part of our overall compensation program in order to align the long-term interests of our employees with those of our stockholders. These awards are made principally under our Equity Incentive Plan, the purpose of which is to secure and retain the services of employees, directors and consultants, and to provide them with incentives to exert maximum efforts for our success by giving them the opportunity through the granting of stock options and other stock awards to benefit from increases in the value of our common stock. The plan, which amends and restates our previous 2000 Equity Incentive Plan, was adopted by our board of directors on February 27, 2009 and approved by our stockholders on April 23, 2009. The proposed amendment to the plan was approved by our board of directors, subject to stockholder approval, on February 16, 2012. The plan currently provides that no more than a total of 35,000,000 shares of our common stock may be issued pursuant to stock awards granted under the plan, of which no more than 3,500,000 shares may be issued pursuant to awards other than stock options and stock appreciation rights. We are asking that stockholders ratify and approve an amendment to the plan (1) increasing the total number of shares that may be issued pursuant to stock awards granted under the plan to 50,000,000 shares and (2) increasing the number of shares that may be issued pursuant to awards other than stock options and stock appreciation rights to 15,000,000 shares in order to maintain the availability to our board of directors of this portion of our overall compensation program.

The terms of the Equity Incentive Plan are summarized below and the complete text of the plan is set forth in Appendix B to this proxy statement, in each case, reflecting the amendment described above.

The Board of Directors recommends that stockholders vote "FOR" the ratification and approval of the amendment to our Equity Incentive Plan.

Administration of the Plan

The plan is administered by our board of directors, or a committee appointed by the board, which determines recipients and types of options and other awards to be granted, including number of shares under the option or other award and when options may be exercised. The compensation committee of the board of directors presently administers the plan.

Awards under the Plan

The plan permits the following types of awards:

- incentive stock options;
- nonstatutory stock options;
- stock bonus awards;
- restricted stock awards;
- phantom stock, or restricted stock unit, awards; and
- stock appreciation rights.

Stock options and other awards granted under the plan are evidenced by agreements that specify the terms and conditions under which they are granted. All stock options and other awards granted under the plan are subject to the terms and conditions contained in the applicable agreement and the plan.

Eligibility

Awards other than incentive stock options may be granted to employees, directors and consultants. Incentive stock options may be granted only to employees. As of February 29, 2012, approximately _____ persons were eligible to participate in the plan, including approximately _____ employees, eight non-employee directors and _____ consultants.

Shares Subject to the Plan

The total number of shares of common stock that may be issued pursuant to stock awards under the plan shall not exceed in the aggregate 50,000,000 shares. No more than 15,000,000 shares may be issued pursuant to awards other than stock options and stock appreciation rights.

If any award expires, lapses, or is terminated or forfeited for any reason, the shares subject to that award will continue to be available for the grant of awards under the plan, provided that shares that are not delivered to the holder of an award because (1) the right to receive such shares is surrendered in a "net exercise" of a stock option or (2) such shares are withheld in satisfaction of the withholding of taxes incurred in connection with the exercise of a stock option or stock appreciation right or the issuance of shares under a stock bonus award, restricted stock award or restricted stock unit award, the surrendered or withheld shares will not be available for subsequent issuance under the plan. Common stock issued as or on the exercise of awards under the plan may be either authorized and unissued shares or reacquired shares.

As of February 29, 2012, there were outstanding under the plan (1) stock options to purchase a total of _____ shares of our common stock, (2) no stock bonus awards, (3) no restricted stock awards, (4) restricted stock unit awards to receive a total of _____ shares of our common stock and (5) no stock appreciation rights. On a pro forma basis to reflect the increase in the number of shares reserved for issuance under the plan, _____ shares remained available for issuance of new stock options or other awards under the plan at that date. Since the founding of our company in 1995, a total of _____ shares of our common stock have been issued under the plan and its predecessors upon the grant, exercise or vesting of stock options and other awards.

Stock Options

The stock options granted under the plan are evidenced by agreements that specify the number of shares of our common stock which may be purchased at a certain specified price and contain other terms and conditions, such as vesting and termination provisions. All stock options granted under the plan are subject to the terms and conditions contained in the applicable stock option agreement and the plan.

Expiration and Termination

The term of each stock option is stated in the applicable stock option agreement. In no event, however, may a stock option be exercised more than ten years after the date the option is granted. In the case of an incentive stock option granted to a 10% stockholder, the maximum term is five years from the date the option is granted.

Option Exercise Price

The exercise price of stock options awarded under the plan is determined by the plan administrator at the time the stock option is awarded. Stock options must have an exercise price that is no less than 100% of the fair market value of our common stock on the date of grant.

The fair market value of a share of common stock on a particular date is equal to the previous day's closing sales price (or the closing bid price, if no sales were reported) of the common stock if the common stock is listed on any established stock exchange or traded on the Nasdaq Stock Market. If there is no regular public trading market for the common stock, the fair market value of the common stock is determined by the board of directors.

Consideration for Exercise of Options

The consideration to be paid for shares to be issued upon exercise of a stock option, including the method of payment, shall be determined by the administrator (and, in the case of an incentive stock option, shall be determined at the time of grant) and may consist entirely of (1) cash or (2), at the discretion of the board of directors, (a) by delivery of other common stock, (b) according to a deferred payment or other similar arrangement, (c) by means of a "net exercise" of the option, or (d) in any other form of legal consideration acceptable to the board.

Stock Bonus Awards and Restricted Stock Awards

The terms and provisions of stock bonus awards and restricted stock awards shall be as set forth in the grant instrument. A stock bonus may be awarded in consideration for past services actually rendered to the company. The purchase price for a

restricted stock award shall be as the administrator shall determine, but not less than 85% of the fair market value on the date the award is granted or the date the purchase is consummated. Shares awarded under a stock bonus or restricted stock award may, but need not be subject to a repurchase or forfeiture right on behalf of the company in accordance with a vesting schedule in the event the participant's employment is terminated.

Phantom Stock Awards and Stock Appreciation Rights

The terms and provisions of phantom stock, or restricted stock unit, awards and stock appreciation rights shall be as set forth in the grant instrument. The price of a common stock equivalent used as the basis from which appreciation is determined for purposes of a stock appreciation right shall be as the administrator shall determine, but not less than 100% of the fair market value on the date the stock appreciation right is granted. Restricted stock unit awards and the exercise value of a stock appreciation right may be paid in shares of common stock, cash, a combination of common stock and cash, or other consideration, as determined by the administrator and set forth in the grant instrument.

Other Provisions

Limits on Transfer of Awards

In general, plan participants may not sell, pledge, assign, transfer or otherwise dispose of any stock options or other awards other than by will or the laws of descent or distribution and the plan participant alone may exercise his stock options or other awards during his lifetime. Awards other than incentive stock options may be transferred only if permitted under the agreement that evidences the terms of the award.

Adjustments on Changes in Capital Structure or on Change of Control

If we effect a stock split, reverse stock split, stock dividend, redemption, combination, reclassification or other similar change affecting our capital stock, adjustments reflecting the change will be made in (1) the aggregate number of shares of common stock authorized for issuance under the plan; (2) the number of shares underlying each outstanding award; and (3) if applicable, the price per share of each award.

If a change in control transaction shall occur, the surviving or acquiring corporation shall assume all awards or provide a substitute similar award. If the surviving or acquiring corporation fails to so provide such assumption or substitution, then awards held by those participants whose employment has not been terminated will be accelerated in full and the awards will subsequently terminate if not exercised. Any other awards outstanding under the plan will terminate if not exercised (if applicable) prior to the event.

Amendment or Termination of the Plan

The board may at any time amend, alter, suspend or discontinue the plan but no amendment, alteration, suspension or discontinuation which would impair your rights under any previous grant may be made without the consent of the participant.

Term of the Plan

No stock options or other awards may be granted under the plan after February 26, 2019.

United States Federal Income Tax Consequences

The following is a brief summary of certain of the federal income tax consequences of certain transactions under the plan based on current federal income tax laws. This summary is not intended to be exhaustive and does not describe state or local tax consequences. Additional or different federal tax consequences to the employee, director or consultant or to our company may result depending on considerations other than those described below.

Nonstatutory Stock Options

In general, optionholders will not recognize any taxable income at the time they are granted nonstatutory stock options. When an optionholder exercises a nonstatutory stock option, he or she will recognize ordinary income measured by the excess of the then fair market value of the shares over the exercise price and we will be entitled to a deduction for a corresponding amount. Different rules apply to options that have a "readily ascertainable fair market value," as that phrase is defined in regulations promulgated under Section 83 of the Internal Revenue Code of 1986. When an optionholder sells or otherwise disposes of shares that were acquired by exercising nonstatutory stock options, any amount that the optionholder receives in excess of the sum of (1) the exercise price of the shares as of the date of exercise and (2) the amount includable in income with respect to such option, if any, such sum being the optionholder's "basis" in the shares,

will, in general, be treated as a long term or short term capital gain, depending on the holding period of the shares. We are not entitled to any tax deduction in connection with an optionholder's sale or disposition of the shares. If an optionholder receives less than his or her basis in the shares, the loss will, in general, be treated as a long term or short term capital loss, depending on the holding period of the shares.

Incentive Stock Options

Optionholders will not be taxed on the grant or exercise of an incentive stock option that qualifies under Section 422 of the Internal Revenue Code, unless an alternative minimum tax liability is triggered. When an optionholder sells or otherwise makes a taxable disposition of shares that he or she acquired by exercising an incentive stock option, the optionholder will recognize a capital gain on the excess of the amount realized on disposition over the exercise price of the incentive stock option, provided that the optionholder has not disposed of the shares until at least two years after the date the option was granted and one year after the date the optionholder exercised the option. Failure to comply with these holding requirements will result in ordinary income treatment for the gain. Unless the optionholder disposes of shares received on exercise of the incentive stock option before meeting the applicable holding period requirements, we will not be entitled to a deduction with respect to the grant or exercise of the incentive stock option. In the event an optionholder makes a "disposition" of the shares received on exercise of an incentive stock option before meeting the two year or one year holding period requirements, the gain on the disposition, to the extent of the lesser of (1) the excess of the fair market value of the shares on the date of exercise over the exercise price or (2) the excess of the amount realized on disposition over the exercise price, will be treated as ordinary income to the optionholder, and we will generally be entitled to a corresponding deduction. The balance of the gain, if any, realized on such a disposition will be treated as long term or short term capital gain, depending on the holding period of the shares. To the extent that an optionholder is entitled to capital gains treatment, we will not be entitled to a corresponding deduction for such gain. If the amount realized at the time of the disposition is less than the exercise price, the optionholder will not be required to treat any amount as ordinary income, provided the disposition is of a type that would give rise to a recognizable loss. In such event, the loss will be treated as a long term or short term capital loss depending on the holding period of the shares.

Stock Bonus Awards

In general, if an individual receives a stock bonus award, he or she will be taxed on the fair market value of the shares on the date the shares are issued. We will be generally entitled to a deduction for a corresponding amount. When a stock bonus award is subject to forfeiture restrictions, an individual will not recognize any taxable income at the time he or she is granted the award, but upon the lapse of the restrictions applicable to such award, that person will recognize ordinary income equal to the fair market value of the shares on the date the restrictions on the award lapsed, and we will be entitled to a deduction for a corresponding amount. If, upon a taxable disposition of the shares, the stockholder receives more or less than his or her basis in the shares, the gain or loss will be a long term or short term capital gain or loss, depending on the holding period of the shares, measured from the date that the receipt of the shares was taxable to the stockholder.

Restricted Stock Awards

In general, an individual will not recognize any taxable income at the time he or she is granted an award of restricted stock, but upon the lapse of the restrictions applicable to such award, that person will recognize ordinary income equal to the fair market value of the shares on the date the restrictions on the award lapsed less the purchase price for such shares, and we will be entitled to a deduction for a corresponding amount. If the stockholder sells or otherwise disposes of such shares in a taxable disposition, the sale or disposition will be subject to the same treatment described above for a taxable disposition of shares acquired upon an exercise of a nonstatutory stock option.

Phantom Stock Awards

In general, an individual will not recognize any taxable income at the time he or she is granted a phantom stock, or restricted stock unit, award. Upon settlement of a restricted stock unit award, the individual will recognize ordinary income equal to the fair market value of the cash or shares actually received by the individual. We will be generally entitled to a deduction for the corresponding amount.

Stock Appreciation Rights

In general, an individual will not recognize any taxable income at the time he or she is granted stock appreciation rights. Upon exercise of a stock appreciation right, the individual will recognize ordinary income equal to the fair

market value of the cash or shares received by the individual upon exercise. We will be generally entitled to a deduction for the corresponding amount.

The foregoing summary does not constitute a definitive statement of the federal income tax effects of awards granted under the Plan.

New Plan Benefits Table

In February 2012, the compensation committee of our board of directors approved a mix of annual stock option grants and restricted stock unit awards under our Equity Incentive Plan to eligible executive officers and other employees, as described below under the heading “Executive and Director Compensation - Compensation Discussion and Analysis - Long-Term Stock-Based Incentive Awards.” The following table presents information regarding the number of annual stock options and the dollar value of annual restricted stock units awarded to the following individuals or groups of individuals in 2012:

- each of the individuals listed in “Executive and Director Compensation - Summary Compensation Table for 2011”;
- all current executive officers, as a group;
- all current directors who are not executive officers, as a group; and
- all non-executive officer employees, including all current officers who are not executive officers, as a group.

The compensation committee retains broad discretion over the granting and amount of awards under our Equity Incentive Plan. As a result, it is not possible to determine any additional benefits or amounts that will be received by any individual participant or group of participants in the future.

| Name and Position | Number of Shares Underlying Stock Options | Dollar Value of Shares Underlying Restricted Stock Units ⁽¹⁾ |
|---|--|--|
| Arthur T. Sands, M.D., Ph.D. President, Chief Executive Officer and Director | 592,000 | \$266,400 |
| Jeffrey L. Wade, J.D. Executive Vice President, Corporate Development and Chief Financial Officer | 312,000 | \$140,400 |
| Alan J. Main, Ph.D. Executive Vice President of Pharmaceutical Research | 280,000 | \$126,000 |
| Brian P. Zambrowicz, Ph.D. Executive Vice President and Chief Scientific Officer | 344,000 | \$154,800 |
| Pablo Lapuerta, M.D. Senior Vice President, Clinical Development and Chief Medical Officer | 208,000 | \$93,600 |
| Executive Group | 1,797,000 | \$829,800 |
| Non-Executive Director Group | — | — |
| Non-Executive Officer Employee Group | 1,214,000 | \$3,472,740 |

(1) Based on the closing price of our common stock on the Nasdaq Global Select Market of \$1.80 per share on February 14, 2012, the last trading day prior to the date of grant

PROPOSAL NUMBER 4:

RATIFICATION AND APPROVAL OF AMENDMENT TO NON-EMPLOYEE DIRECTORS' STOCK OPTION PLAN

We currently use stock option awards as a part of our overall compensation program in order to align the long-term interests of the non-employee members of our board of directors with those of our stockholders. These awards are made under our Non-Employee Directors' Stock Option Plan, the purpose of which is to secure and retain the services of non-employee directors, and to provide them with incentives to exert maximum efforts for our success by giving

them the opportunity through the granting of nonstatutory stock options to benefit from increases in the value of our common stock. The plan, which amends and restates our previous 2000 Non-Employee Directors' Stock Option Plan, was adopted by our board of directors on February 27, 2009 and approved by our stockholders on April 23, 2009. The proposed amendment to the plan was approved by our board of directors, subject to stockholder approval, on February 16, 2012.

12

The plan currently provides that no more than a total of 1,200,000 shares of our common stock may be issued pursuant to stock options granted under the plan and that non-employee directors who have served in such capacity for six months shall be granted an annual option to purchase 10,000 shares of common stock (or 20,000 shares, in the case of the non-employee chairman of our board of directors). We are asking that stockholders ratify and approve an amendment to the plan (1) increasing the total number of shares of our common stock that may be issued pursuant to stock awards granted under the plan to 1,500,000 shares, (2) expanding the types of potential awards under the plan to include restricted stock awards, (3) replacing the current annual option grant with an annual option grant to purchase 20,000 shares and an annual grant of restricted stock with a fair market value of \$20,000 and (4) renaming the plan the Non-Employee Directors' Equity Incentive Plan, with the objective of encouraging the ownership of our common stock by members of our board of directors, ensuring that this portion of our overall compensation program remains competitive in comparison to the compensation programs of our peer group companies and maintaining the availability to our board of directors of this portion of our overall compensation program.

The terms of the Non-Employee Directors' Stock Option Plan are summarized below and the complete text of the plan is set forth in Appendix C to this proxy statement, in each case, reflecting the amendment described above.

The Board of Directors recommends that stockholders vote "FOR" the ratification and approval of the amendment to our Non-Employee Directors' Stock Option Plan.

Administration of the Plan

The plan is administered by our board of directors, which oversees the grant of options under the plan and determines the provisions of each option granted, to the extent not specified in the plan.

Awards under the Plan

The plan permits the award of nonstatutory stock options and restricted stock awards. Stock options and restricted stock awards granted under the plan are evidenced by agreements that specify the terms and conditions under which they are granted. All stock options and restricted stock awards granted under the plan are subject to the terms and conditions contained in the applicable agreement and the plan.

Eligibility

Stock options and restricted stock awards are granted to non-employee directors under the plan. Upon the date of his or her initial election or appointment to the board of directors, each non-employee director is granted an option to purchase 30,000 shares of our common stock. Further, on the day following each annual meeting of stockholders, each person who is then a non-employee director and has been a non-employee director for at least six months is granted an option to purchase 20,000 shares of our common stock and a restricted stock award of the number of shares of our common stock having a fair market value on the date of grant of \$20,000, rounded down to the nearest whole share number. Eight of the nine members of our board of directors are currently eligible to participate in the plan.

Shares Subject to the Plan

The total number of shares of common stock that may be issued pursuant to stock awards under the plan shall not exceed in the aggregate 1,500,000 shares.

If any award expires, lapses, or is terminated or forfeited for any reason, the shares subject to that award will continue to be available for the grant of awards under the plan. Common stock issued as or on the exercise of awards under the plan may be either authorized and unissued shares or reacquired shares.

As of February 29, 2012, there were outstanding under the plan (1) options to purchase a total of 698,000 shares of our common stock and (2) no restricted stock awards. On a pro rata basis to reflect the increase in the number of shares reserved for issuance under the plan, 802,000 shares remained available for issuance of new stock options or restricted stock awards under the plan at that date. To date, no shares have been issued under the plan and its predecessors upon the exercise or grant of stock options or restricted stock awards.

Stock Options

The stock options granted under the plan are evidenced by agreements that specify the number of shares of our common stock which may be purchased at a certain specified price and contain other terms and conditions, such as vesting and termination provisions. All stock options granted under the plan are subject to the terms and conditions contained in the applicable stock option agreement and the plan.

Vesting and Exercisability

Stock options granted under the plan “vest,” or become exercisable, as follows:

• Initial grants of options to purchase 30,000 shares of our common stock provide for vesting of 1/60th of the shares subject to the option each month after grant for five years after the date of grant.

• Annual grants of options to purchase 20,000 shares of our common stock provide for vesting of 1/12th of the shares subject to the option each month after grant for twelve months after the date of the grant.

Expiration and Termination

Stock options granted under the plan have a term of ten years from the date of grant, subject to earlier termination upon the occurrence of certain events. In no event, however, may a stock option be exercised more than ten years after the date the option is granted.

Option Exercise Price

Stock options awarded under the plan have an exercise price of 100% of the fair market value of our common stock on the date of grant. The fair market value of a share of common stock on a particular date is equal to the previous day's closing sales price (or the closing bid price, if no sales were reported) of the common stock if the common stock is listed on any established stock exchange or traded on the Nasdaq Stock Market. If there is no regular public trading market for the common stock, the fair market value of the common stock is determined by our board of directors.

Consideration for Exercise of Options

The consideration to be paid for shares to be issued upon exercise of a stock option, including the method of payment, may be paid, to the extent permitted by law, in any combination of (1) cash, (2) delivery of other shares of our common stock, or (3) by “net exercise” of the stock option.

Restricted Stock Awards

The terms and provisions of restricted stock awards shall be as set forth in the grant instrument. The number of shares subject to each restricted stock award is determined by dividing \$20,000 by the fair market value of our common stock on the date of grant, rounded down to the nearest whole share number. The fair market value of a share of common stock on a particular date is equal to the previous day's closing sales price (or the closing bid price, if no sales were reported) of the common stock if the common stock is listed on any established stock exchange or traded on the Nasdaq Stock Market. If there is no regular public trading market for the common stock, the fair market value of the common stock is determined by our board of directors. All of the shares subject to restricted stock awards are fully vested on the date of grant and are subject to certain restrictions on sale prohibiting any non-employee director from selling such shares while a member of our board of directors.

Other Provisions

Limits on Transfer of Awards

In general, non-employee directors may not sell, pledge, assign, transfer or otherwise dispose of any stock options or restricted stock awards other than (i) by will or the laws of descent or distribution, (ii) in certain circumstances, by instrument to an inter vivos or testamentary trust and (iii) by gift to a member of such non-employee director's immediate family.

Adjustments on Changes in Capital Structure or on Change of Control

If we effect a stock split, reverse stock split, stock dividend, redemption, combination, reclassification or other similar change affecting our capital stock, adjustments reflecting the change will be made in (1) the aggregate number of shares of common stock authorized for issuance under the plan; (2) the number of shares underlying each outstanding award; and (3) if applicable, the exercise price per share subject to each outstanding stock option.

If a change in control transaction shall occur, the surviving or acquiring corporation shall assume all awards or provide or substitute similar awards. If the surviving or acquiring corporation refuses to so provide such assumption or substitution, then the vesting of awards granted under the plan will be accelerated in full and the awards will subsequently terminate if not exercised, as applicable.

If a change in control transaction shall occur and the surviving or acquiring corporation assumes the awards granted under the plan, but any non-employee director is not elected or appointed to the board of directors of the surviving or acquiring corporation, then the vesting of that non-employee director's awards shall be accelerated by 18 months.

Amendment or Termination of the Plan

The board of directors may at any time amend, alter, suspend or discontinue the plan but no amendment, alteration, suspension or discontinuation which would impair the rights of a non-employee director under any previous grant may be made without such non-employee director's consent.

Term of the Plan

No stock options or restricted stock awards may be granted under the plan after February 26, 2019.

United States Federal Income Tax Consequences

The following is a brief summary of certain of the federal income tax consequences of certain transactions under the plan based on current federal income tax laws. This summary is not intended to be exhaustive and does not describe state or local tax consequences. Additional or different federal tax consequences to the non-employee director or to us may result depending on considerations other than those described below.

Nonstatutory Stock Options

In general, optionholders will not recognize any taxable income at the time they are granted a nonstatutory stock option. When an optionholder exercises a nonstatutory stock option, he or she will recognize ordinary income measured by the excess of the then fair market value of the shares over the exercise price and we will be entitled to a deduction for a corresponding amount. Different rules apply to options that have a "readily ascertainable fair market value," as that phrase is defined in regulations promulgated under Section 83 of the Internal Revenue Code of 1986. When an optionholder sells or otherwise disposes of shares that were acquired by exercising a nonstatutory stock option, any amount the optionholder receives in excess of the sum of (1) the exercise price of the shares as of the date of exercise and (2) the amount includable in income with respect to such option, if any, such sum being the optionholder's "basis" in the shares, will, in general, be treated as a long term or short term capital gain, depending on the holding period of the shares. We are not entitled to any tax deduction in connection with an optionholder's sale or disposition of the shares. If an optionholder receives less than his or her basis in the shares, the loss will, in general, be treated as a long term or short term capital loss, depending on the holding period of the shares.

Restricted Stock Awards

In general, an individual will not recognize any taxable income at the time he or she is granted an award of restricted stock, but upon the lapse of the restrictions applicable to such award, that person will recognize ordinary income equal to the fair market value of the shares on the date the restrictions on the award lapsed less the purchase price for such shares, and we will be entitled to a deduction for a corresponding amount. If the stockholder sells or otherwise disposes of such shares in a taxable disposition, the sale or disposition will be subject to the same treatment described above for a taxable disposition of shares acquired upon an exercise of a nonstatutory stock option.

The foregoing summary does not constitute a definitive statement of the federal income tax effects of stock options granted under the plan.

New Plan Benefits Table

The following table presents information regarding the number of annual stock options and restricted stock awards that we anticipate will be awarded under our Non-Employee Directors' Stock Option Plan in 2012 to the following individuals or groups of individuals, in each case reflecting the amendment described above:

- each of the individuals listed in "Executive and Director Compensation - Summary Compensation Table for 2011";
- all current executive officers, as a group;
- all current directors who are not executive officers, as a group; and
- all non-executive officer employees, including all current officers who are not executive officers, as a group.

| Name and Position | Number of Shares Underlying Stock Options | Dollar Value of Shares Underlying Restricted Stock Awards |
|--|---|---|
| Arthur T. Sands, M.D., Ph.D. President, Chief Executive Officer and Director | — | — |
| Jeffrey L. Wade, J.D. Executive Vice President, Corporate Development and Chief Financial Officer | — | — |
| Alan J. Main, Ph.D. Executive Vice President of Pharmaceutical Research | — | — |
| Brian P. Zambrowicz, Ph.D. Executive Vice President and Chief Scientific Officer | — | — |
| Pablo Lapuerta, M.D. Senior Vice President, Clinical Development and Chief Medical Officer | — | — |
| Executive Group | — | — |
| Non-Executive Director Group | 160,000 | \$ 160,000 |
| Non-Executive Officer Employee Group | — | — |

PROPOSAL NUMBER 5:**ADVISORY VOTE ON EXECUTIVE COMPENSATION**

The Dodd-Frank Wall Street Reform and Consumer Protection Act 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 2012 annual meeting of stockholders pursuant to the compensation disclosure rules of the Securities and Exchange Commission, including the Compensation Discussion and Analysis, 2011 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 6:

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, 2012, 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, 2012.

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, | |
|-----------------------------------|--------------------------|-----------|
| | 2011 | 2010 |
| Audit fees ⁽¹⁾ | \$384,500 | \$479,700 |
| Audit-related fees ⁽²⁾ | 25,000 | 24,000 |
| Tax fees | — | — |
| All other fees | — | — |
| | \$409,500 | \$503,700 |

“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, 2010 and 2011, (ii) the audit of our annual financial statements for the fiscal years ended December 31, 2010 and 2011, (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.

(1) “Audit-related fees” include assurance or related services reasonably related to our audit for the fiscal years ended December 31, 2010 and 2011. 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 non-audit 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 Statement on Auditing Standards No. 61, Communication 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, 2011.

Audit Committee

Samuel L. Barker, Ph.D. (Chairman)

Frank P. Palantoni

Judith L. Swain, M.D.

17

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 compensation 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 February 29, 2012 by:

- each of the individuals listed in “Executive and Director Compensation - Summary Compensation Table for 2011”;
- each of our directors;
- each person, or group of affiliated persons, who is known by us to own beneficially five percent or more 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 options held by that person that are currently exercisable or exercisable within 60 days of February 29, 2012 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 _____ shares of common stock outstanding on February 29, 2012.

Unless otherwise indicated in the footnotes, the address of each of the individuals named below is: c/o Lexicon Pharmaceuticals, Inc., 8800 Technology Forest Place, The Woodlands, Texas 77381.

| | Beneficial Ownership | | |
|---|-------------------------------------|---|----------------------|
| | Number of Shares Beneficially Owned | Shares Issuable Pursuant to Options Exercisable within 60 Days of February 29, 2012 | Percentage Ownership |
| Invus, L.P., Invus Public Equities, L.P., Invus C.V. and related parties ⁽¹⁾ | 280,154,744 | | % |
| FMR LLC and related parties ⁽²⁾ | 66,078,981 | | % |
| Arthur T. Sands, M.D., Ph.D. ⁽³⁾ | | | % |
| Jeffrey L. Wade, J.D. | | | * |
| Alan J. Main, Ph.D. | | | * |
| Brian P. Zambrowicz, Ph.D. | | | * |
| Pablo Lapuerta, M.D. | | | * |
| Raymond Debbane ⁽⁴⁾ | | | % |
| Philippe J. Amouyal | | | * |
| Samuel L. Barker, Ph.D. | | | * |
| Robert J. Lefkowitz, M.D. | | | * |
| Alan S. Nies, M.D. | | | * |
| Frank P. Palantoni | | | * |
| Christopher J. Sobecki | | | * |
| Judith L. Swain, M.D. | | | * |
| All current directors and executive officers as a group ⁽³⁾⁽⁴⁾ (14 persons) | | | % |

* Represents beneficial ownership of less than 1 percent.

⁽¹⁾ Based upon a Schedule 13D/A filed with the SEC on December 27, 2011, reflecting the beneficial ownership of our common stock by Invus, L.P., Invus Public Equities, L.P., Invus C.V. and related parties. Invus, L.P. and related parties may be deemed to have sole investment and voting power with respect to 244,818,843 of such shares and shared voting power with respect to 5,553,292 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 5,553,292 of such shares. Invus C.V. and related parties may be deemed to have sole investment and voting power with respect to 29,782,609 of such shares. The address for Invus, L.P. and Invus Public Equities, L.P. is Clarendon House, 2

Church Street, Hamilton HM II, Bermuda. The address for Invus C.V. is Marten Meesweg 25, Rotterdam 3068 AV, Netherlands. The address for all related parties is 750 Lexington Avenue, 30th Floor, New York, New York 10022.

(2) Based upon a Schedule 13G/A filed with the SEC on February 14, 2012, reflecting the beneficial ownership of our common stock by FMR LLC and related parties. FMR LLC and Edward C. Johnson 3d each have sole investment power with respect to the shares. The address for FMR LLC and all related parties is 82 Devonshire Street, Boston, Massachusetts 02109.

(3) The number of shares beneficially owned by Dr. Sands includes 60,000 shares held in the name of minor children and 817,500 shares owned by Sands Associates LP. The general partners of Sands Associates LP are ATS Associates, L.L.C., owned by Dr. Sands, and MES Associates, L.L.C., owned by Dr. Sands' wife.

(4) Based upon a Schedule 13D/A filed with the SEC on December 27, 2011, reflecting the beneficial ownership by Mr. Debbane of the shares of our common stock beneficially owned by Invus, L.P., Invus Public Equities, L.P., Invus C.V. and related parties. Mr. Debbane disclaims beneficial ownership of these shares. The address for Mr. Debbane is c/o The Invus Group, LLC, 750 Lexington Avenue, 30th Floor, New York, New York 10022.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors and executive officers, and persons who own more than 10% of our common stock, to file initial reports of ownership and reports of changes in ownership of our common stock with the Securities and Exchange Commission. Directors, executive officers and greater than 10% stockholders are required by Securities and Exchange Commission regulations to furnish us with copies of all such forms that they file. To our knowledge, based solely on our review of the copies of such reports received by us and on written representations by certain reporting persons that no reports on Form 5 were required, we believe that during the fiscal year ended December 31, 2011, all Section 16(a) filing requirements applicable to our executive officers, directors and 10% stockholders were complied with in a timely manner.

EQUITY COMPENSATION PLAN INFORMATION

The following table presents aggregate summary information as of December 31, 2011 regarding the common stock that may be issued upon exercise of options, warrants and rights under all of our existing equity compensation plans, including our Equity Incentive Plan and Non-Employee Directors' Stock Option Plan.

| Plan Category | (a) Number of securities to be issued upon exercise of outstanding options, warrants and rights | (b) Weighted average exercise price per share of outstanding options, warrants and rights ⁽²⁾ | (c) 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⁾ | 22,953,755 | \$2.8431 | 8,054,863 |
| Equity compensation plans not approved by security holders | — | — | — |
| Total | 22,953,755 | \$2.8431 | 8,054,863 |

⁽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 Equity Incentive Plan and Non-Employee Directors' Stock Option 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 Equity Incentive Plan and Non-Employee Directors' Stock Option Plan and excludes from such calculation restricted stock units granted under our 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 our consulting agreements with Robert J. Lefkowitz, M.D., under which Dr. Lefkowitz serves as a consultant to us on matters relating to our drug discovery and development efforts, and with Alan S. Nies, M.D., under which Dr. Nies serves as chairman of our medical advisory board. With respect to Raymond Debbane, Philippe J. Amouyal and Christopher J. Sobecki, the board of directors also considered the percentage of our outstanding common stock owned by Invus and its affiliates.

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 and monitors the integrity of our financial statements, reviews our internal accounting procedures and oversees the qualifications, independence and performance of our independent auditors. The audit committee operates pursuant to a charter that was last amended and restated by the board of directors on October 26, 2005, 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 evaluates the performance of management, determines the compensation of our executive officers and reviews general policy relating to compensation and benefits of our employees. The compensation committee also administers the issuance of stock options, restricted stock units and other awards under our Equity Incentive Plan. The compensation committee operates pursuant to a charter that was approved by the board of directors on February 11, 2004, 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 2011 compensation matters. The compensation committee may retain compensation consultants or other advisors to assist in its evaluation of executive compensation. Although the compensation committee has engaged consultants to advise the committee on matters relating to executive compensation in prior years, the compensation committee did not engage any consultants with respect to 2011 compensation matters.

The compensation committee meets in connection with most regularly scheduled meetings of the board of directors, and holds at least two meetings after the commencement of each year specifically devoted to making compensation decisions regarding the year just ended. In preparation for such decisions, our president and chief executive officer reviews the performance of executive 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 in the absence of management.

The current members of our compensation committee are Mr. Palantoni (chair), Philippe J. Amouyal, Samuel L. Barker, Ph.D. and Alan S. Nies, M.D. The board of directors, in its business judgment, has determined that Mr. Palantoni, Mr. Amouyal, Dr. Barker and Dr. Nies 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 and Dr. Nies described under the heading “Corporate Governance - Independence of the

Board of Directors.”

Corporate Governance Committee. Our corporate governance committee identifies individuals qualified to become members of our board of directors, selects candidates or nominees for director positions to be filled by the board of directors or

21

our stockholders and develops appropriate corporate governance principles. The corporate governance committee operates pursuant to a charter that was approved by the board of directors on February 11, 2004, 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 8800 Technology Forest Place, 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 and Dr. Lefkowitz described under the heading "Corporate Governance - Independence of the Board of Directors."

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 2011

The board of directors met seven times in 2011. In 2011, the audit committee met six 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 2011, none of our 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. Eight of the nine members of our board of directors attended our 2011 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.

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 8800 Technology Forest Place, The Woodlands, Texas 77381, Attn: Board of Directors or any individual director.

Compensation Committee Interlocks and Insider Participation

During 2011, Frank P. Palantoni, Philippe J. Amouyal and Alan S. Nies, M.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 2011, 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. purchased 50,824,986 shares of our common stock in August 2007. In November 2011, Invus, exercised its rights under the securities purchase agreement to require us to conduct a pro rata rights offering to our stockholders. In December 2011, we completed the sale of an aggregate of 142,492,883 shares of our common stock in the rights offering, of which 115,044,247 shares were purchased by Invus and its affiliates.

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 and its affiliates, rounded up to the nearest whole number of directors, and pursuant to which Invus has designated Raymond Debbane, Philippe J.

Amouyal and Christopher J. Sobecki. Mr. Debbane is president and chief executive officer of The Invus Group, LLC, an affiliate of Invus, and Mr. Amouyal and Mr. Sobecki are each managing directors of The Invus Group, LLC. 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, to the extent permitted by applicable law and the rules and regulations of the Nasdaq Stock Market. Mr. Amouyal currently serves as a member of our compensation committee and Mr. Debbane currently serves as chairman of our corporate governance committee.

Invus' rights with respect to the designation of 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 the provisions containing these rights at any time in its discretion.

Preemptive Rights. Invus has preemptive rights under the stockholders' agreement to participate in future equity issuances by us, subject to certain exceptions, so as to maintain its then-current percentage ownership of our capital stock. Subject to certain limitations, Invus will be required to exercise its preemptive rights in advance with respect to certain marketed offerings, in which case it will be obligated to buy its pro rata share of the number of shares being offered in such marketed offering, including any over-allotment (or such lesser amount specified in its exercise of such rights), so long as the sale of the shares were priced within a range within 10% above or below the market price on the date we notified Invus of the offering and we met certain other conditions.

The provisions of the stockholders' agreement relating to preemptive rights will terminate on the earlier to occur of August 28, 2017 and the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%.

Consent Rights. Invus is entitled to certain consent rights under the stockholders' agreement, including with respect to (a) the creation or issuance of any new class or series of shares of our capital stock (or securities convertible into or exercisable for shares of our capital stock) having rights, preferences or privileges senior to or on parity with our common stock, (b) any amendment to our certificate of incorporation or bylaws, or amendment to the certificate of incorporation or bylaws of any of our subsidiaries, in a manner adversely affecting Invus' rights under the securities purchase agreement and the related agreements, (c) the repurchase, retirement, redemption or other acquisition of our or our subsidiaries' capital stock (or securities convertible into or exercisable for shares of our or our subsidiaries' capital stock), (d) any increase in the size of our board of directors to more than 12 members and (e) the adoption or proposed adoption of any stockholders' rights plan, "poison pill" or other similar plan or agreement, unless Invus is exempt from the provisions of such plan or agreement.

The provisions of the stockholders' agreement relating to consent rights will terminate on the earlier to occur of August 28, 2017 and the date on which Invus and its affiliates hold less than 15% of the total number of outstanding shares of our common stock.

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 and its affiliates have certain demand and piggyback registration rights with respect to shares of our common stock held by them.

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 and 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 survey data from several sources, relying principally on 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 number of employees, revenues, stage of development, and market capitalization. In general, we have included companies in this comparison group only if they have internal discovery capabilities and efforts.

For compensation decisions made in February 2009, this group of companies consisted of:

| | | |
|-----------------------------|--------------------------------|---------------------------|
| Affymax, Inc. | Human Genome Sciences, Inc. | Medarex, Inc. |
| Arena Pharmaceuticals, Inc. | Incyte Corporation | Rigel Pharmaceuticals Inc |
| Array Biopharma Inc. | Infinity Pharmaceuticals, Inc. | ZymoGenetics, Inc. |
| Exelixis, Inc. | | |

For compensation decisions made in February 2010, this group of companies consisted of:

| | | |
|-----------------------------|-----------------------------|--------------------------------|
| Affymax, Inc. | Exelixis, Inc. | Infinity Pharmaceuticals, Inc. |
| Arena Pharmaceuticals, Inc. | Human Genome Sciences, Inc. | Rigel Pharmaceuticals Inc |
| Array Biopharma Inc. | Incyte Corporation | ZymoGenetics, Inc. |

For compensation decisions made in February 2011, this group of companies consisted of:

| | | |
|-------------------------------|-------------------------------------|---------------------------------|
| Acorda Therapeutics, Inc. | Dyax Corp. | Orexigen Therapeutics, Inc. |
| Affymax, Inc. | Exelixis, Inc. | Peregrine Pharmaceuticals, Inc. |
| Allos Therapeutics, Inc. | Facet Biotech Corporation | QLT Inc. |
| Alnylam Pharmaceuticals, Inc. | Geron Corporation | Rigel Pharmaceuticals Inc |
| Amag Pharmaceuticals, Inc. | ImmunoGen, Inc. | Sangamo Biosciences, Inc. |
| Ardea Biosciences, Inc. | Incyte Corporation | Seattle Genetics, Inc. |
| Arena Pharmaceuticals, Inc. | Infinity Pharmaceuticals, Inc. | Siga Technologies, Inc. |
| Ariad Pharmaceuticals, Inc. | Inspire Pharmaceuticals, Inc. | Spectrum Pharmaceuticals, Inc. |
| Array Biopharma Inc. | Intermune, Inc. | Targacept, Inc. |
| Avanir Pharmaceuticals, Inc. | Ligand Pharmaceuticals Incorporated | Xenoport, Inc. |
| Cell Therapeutics, Inc. | Nektar Therapeutics | ZymoGenetics, Inc. |
| Cytori Therapeutics, Inc. | Optimer Pharmaceuticals, Inc. | |

For compensation decisions made in February 2012, this group of companies consisted of:

| | | |
|-------------------------------|----------------------------------|-------------------------------|
| Acorda Therapeutics, Inc. | Dyx Corp. | Micromet, Inc. |
| Allos Therapeutics, Inc. | Dynavax Technologies Corporation | Neurocrine Biosciences, Inc. |
| Alnylam Pharmaceuticals, Inc. | Exelixis, Inc. | NPS Pharmaceuticals, Inc. |
| Amag Pharmaceuticals, Inc. | Geron Corporation | Optimer Pharmaceuticals, Inc. |
| Ardea Biosciences, Inc. | Idenix Pharmaceuticals, Inc. | Pharmasset, Inc. |
| Arena Pharmaceuticals, Inc. | ImmunoGen, Inc. | QLT Inc. |
| Ariad Pharmaceuticals, Inc. | Immunomedics, Inc. | Rigel Pharmaceuticals Inc |
| Arqule, Inc. | Inspire Pharmaceuticals, Inc. | Sangamo Biosciences, Inc. |
| Avanir Pharmaceuticals, Inc. | Ironwood Pharmaceuticals, Inc. | Synta Pharmaceuticals Corp. |
| AVEO Pharmaceuticals, Inc. | Isis Pharmaceuticals, Inc. | Targacept, Inc. |
| Cell Therapeutics, Inc. | MannKind Corporation | Xenoport, Inc. |
| Cytori Therapeutics, Inc. | Medivation, 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. In general, the compensation committee has employed the 50th and 60th percentile of the broad survey data, with reference to medians and averages reported by the selected group of biopharmaceutical companies, in evaluating base salaries and bonus targets. 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. Among the challenges faced by us and other companies in the biopharmaceutical industry is the unique combination of the relatively long time period typically necessary to discover, develop and commercialize drugs and the historically low success rate in doing so. As a result, in evaluating the performance of management, the compensation committee takes into consideration such factors as 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 company and individual performance over the preceding year, as well as prevailing financial conditions. The compensation committee typically meets several times 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 or other advisors when it deems appropriate to assist in its evaluation of executive compensation. The compensation committee did not engage any consultants with respect to 2009, 2010 or 2011 compensation matters.

We received a favorable advisory vote on the compensation of our named executive officers at our 2011 annual meeting of stockholders, with over 80% 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 on executive compensation when making future decisions with respect to the compensation paid to our named executive officers.

Corporate and Individual Performance Criteria

February 2009 Compensation Determinations

In February 2009, the compensation committee made determinations regarding 2008 cash bonus awards and 2009 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2008:

- the completion of a Phase 2a clinical trial of our LX6171 drug candidate in subjects with age-associated memory impairment, but without demonstrating significant effects on the parameters of attention or memory that were evaluated;
- the completion of Phase 1 clinical trials of another drug candidate, LX1031, and commencement of dosing in a Phase 2a clinical trial in patients with irritable bowel syndrome;
- the completion of Phase 1a and Phase 1b clinical trials of a third drug candidate, LX2931;
- the completion of Phase 1a and Phase 1b clinical trials of a fourth drug candidate, LX1032;
- the submission of an investigational new drug application for one of our other drug candidates, LX4211;
- our progress relative to our objectives in advancing our other drug discovery and development programs; and
- our performance relative to our objectives for our net use of cash in operations, capital expenditures and year-end cash and investments.

The committee's compensation determinations in February 2009 reflected its assessment that we partially achieved our objectives relating to our drug discovery and development programs, collectively representing what the committee considered to be our most important objectives, and achieved our objectives relating to net use of cash in operations, capital expenditures and year-end cash and investments. Taking into account the balance of factors described above, it was the committee's assessment that our overall corporate objectives were partially achieved.

For executive officers other than Dr. Sands, our president and chief executive officer, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each executive officer towards the achievement of the year's corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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. Dr. Sands had no individual goals for 2008 apart from the corporate goals.

The committee's determinations for Dr. Sands 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 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 executive officer's individual contributions towards the achievement of such corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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 such determinations. In the case of Dr. Main, the compensation committee took into account his contributions toward the achievement of an investigational new drug application for LX4211, the selection of an additional drug candidate, LX7101, and progress in additional drug discovery programs, as well as his strategic and operational leadership. In the case of Mr. Wade, the compensation committee took into account his contributions in overseeing financial and legal matters and business development activities, as well as his strategic and operational leadership. In the case of Dr. Zambrowicz, the compensation committee took into account his contributions toward the achievement of an investigational new drug application for LX4211, the selection of an additional drug candidate, LX7101, and progress in additional drug discovery programs, as well as his strategic and operational leadership and participation in business development activities.

February 2010 Compensation Determinations

In February 2010, the compensation committee made determinations regarding 2009 cash bonus awards and 2010 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2009:

- the completion of a Phase 2a clinical trial of our LX1031 drug candidate in patients with irritable bowel syndrome, with favorable results;

the initiation and completion of a Phase 1 clinical trial of another drug candidate, LX4211, and the initiation and completion of a Phase 2a clinical trial of LX4211 in patients with Type 2 diabetes, with favorable results; the initiation and completion of a drug interaction study of a third drug candidate, LX2931, and the initiation of a Phase 2a clinical trial of LX2931 in patients with rheumatoid arthritis; the initiation of a Phase 2a clinical trial of a fourth drug candidate, LX1032, in patients with carcinoid syndrome; our progress relative to our objectives in advancing our other drug discovery and development programs; our performance relative to our objectives for financial performance, specifically relating to year-end cash and investments and business development; and our performance relative to our objectives relating to company culture and leadership, including retention.

The committee's compensation determinations in February 2010 reflected its assessment that we largely achieved our objectives relating to our drug discovery and development programs, collectively representing what the committee considered to be our most important objectives, and partially achieved our objectives relating to financial performance and company culture and leadership. Taking into account the balance of factors described above, it was the committee's assessment that our overall corporate objectives were largely achieved.

For executive officers other than Dr. Sands, our president and chief executive officer, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each executive officer towards the achievement of the year's corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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. Dr. Sands had no individual goals for 2009 apart from the corporate goals.

The committee's determinations for Dr. Sands 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 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 executive officer's individual contributions towards the achievement of such corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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 such determinations. In the case of Dr. Main, the compensation committee took into account his contributions toward activities supporting the advancement of our drug candidates in clinical development and progress in our drug discovery programs, as well as his strategic and operational leadership. In the case of Mr. Wade, the compensation committee took into account his contributions toward the completion of a common stock financing and business development and alliance management activities, as well as his strategic and operational leadership. In the case of Dr. Zambrowicz, the compensation committee took into account his contributions toward the advancement of our drug candidates in clinical development with favorable results and progress in our drug discovery programs, as well as his strategic and operational leadership and participation in business development activities.

February 2011 Compensation Determinations

In February 2011, the compensation committee made determinations regarding 2010 cash bonus awards and 2011 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2010:

the progression in the clinical development of our LX4211 drug candidate, including the initiation and completion of a mechanistic clinical study of a tablet formulation of LX4211 in patients with Type 2 diabetes, with favorable results; the completion of a Phase 2a clinical trial of a second drug candidate, LX2931, in patients with rheumatoid arthritis, with results suggesting that patients treated with the highest dose level of LX2931 studied in the clinical trial showed improvement in the primary efficacy endpoint of the study;

the progression of enrollment in a Phase 2a clinical trial of a third drug candidate, LX1032, in patients with carcinoid syndrome;

the progression of our efforts to develop an improved formulation of a fourth drug candidate, LX1031, for irritable bowel syndrome and the submission of an investigational new drug application for LX1033, a back-up compound to LX1031;

our progress relative to our objectives in advancing our other drug discovery and development programs; our exercise of a restructured purchase option under our financing arrangement with Symphony Icon Holdings LLC to acquire all the equity of Symphony Icon, Inc., thereby reacquiring all the rights to LX1031, LX1032, LX1033 and the other drug programs subject to the collaboration; and our performance relative to our objectives for financial performance, specifically relating to year-end cash and investments and business development.

The committee's compensation determinations in February 2011 reflected its assessment that we partially achieved our objectives relating to both our drug discovery and development programs, collectively representing what the committee considered to be our most important objectives, 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 executive officers other than Dr. Sands, our president and chief executive officer, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each executive officer towards the achievement of the year's corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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. Dr. Sands had no individual goals for 2010 apart from the corporate goals.

The committee's determinations for Dr. Sands 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 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 executive officer's individual contributions towards the achievement of such corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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 such determinations. In the case of Dr. Main, the compensation committee took into account his contributions toward the achievement of an investigational new drug application for LX1033, the selection of two additional drug candidates, LX5061 and LX2311, and progress in additional drug discovery programs, as well as his strategic and operational leadership. In the case of Mr. Wade, the compensation committee took into account his contributions toward the completion of a common stock financing, our exercise of the restructured purchase option under our financing arrangement with Symphony Icon Holdings LLC and our business development and alliance management activities, as well as his strategic and operational leadership. In the case of Dr. Zambrowicz, the compensation committee took into account his contributions toward the advancement of our drug candidates in clinical development, with favorable results in clinical trials of LX4211, the achievement of an investigational new drug application for LX1033, the selection of two additional drug candidates, LX5061 and LX2311, and progress in additional drug discovery programs, as well as his strategic and operational leadership and participation in business development activities.

February 2012 Compensation Determinations

In February 2012, the compensation committee made determinations regarding 2011 cash bonus awards and 2012 base salaries, bonus targets and long-term stock-based incentive awards, taking into account the following factors in its evaluation of corporate performance in 2011:

the progression in the clinical development of our LX4211 drug candidate, including the initiation and timely progression of enrollment for a Phase 2b clinical trial of LX4211 and the initiation and completion of two other clinical studies, one of which tested the combined effects of LX4211 with sitagliptin, each with positive results; the completion of a Phase 2a clinical trial of a second drug candidate, LX1032, in patients with carcinoid syndrome, with positive results, and the initiation of a proof-of-concept clinical study of LX1032 in patients with inflammatory bowel disease;

the completion of a Phase 1 clinical trial of a third drug candidate, LX1033 for irritable bowel syndrome, with positive results, and the progression of preparations for a Phase 2a clinical trial of LX1033 in irritable bowel syndrome patients;

the initiation of a dose escalation clinical study of a fourth drug candidate, LX2931, in patients with rheumatoid arthritis;

the submission of an investigational new drug application for one of our other drug candidates, LX7101 for glaucoma;

30

our progress relative to our objectives in advancing our other drug discovery and development programs; and our performance relative to our objectives for financial performance, specifically relating to year-end cash and investments and business development.

The committee's compensation determinations in February 2012 reflected its assessment that we largely achieved our objectives relating to our drug discovery and development programs, collectively representing what the committee considered to be our most important objectives, and partially achieved our objectives relating to 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 executive officers other than Dr. Sands, our president and chief executive officer, the compensation committee also took into account individual goals, which consisted principally of the expected individual contributions of each executive officer towards the achievement of the year's corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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. Dr. Sands had no individual goals for 2011 apart from the corporate goals.

The committee's determinations for Dr. Sands 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 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 executive officer's individual contributions towards the achievement of such corporate goals, together with Dr. Sands' and the committee's independent assessment of each 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 such determinations. In the case of Dr. Main, the compensation committee took into account his contributions toward the achievement of an investigational new drug application for LX7101 and progress in additional drug discovery programs, as well as his strategic and operational leadership. In the case of Mr. Wade, the compensation committee took into account his contributions toward our financial management and our business development and alliance management activities, as well as his strategic and operational leadership. In the case of Dr. Zambrowicz, the compensation committee took into account his contributions toward the advancement of our drug candidates in clinical development, with favorable results in clinical trials of LX4211, LX1032 and LX1033, the achievement of an investigational new drug application for LX7101, and progress in additional drug discovery programs, as well as his strategic and operational leadership and participation in business development activities. In the case of Dr. Lapuerta, the compensation committee took into account his contributions toward the advancement of our drug candidates in clinical development, with favorable results in clinical trials of LX4211, LX1032 and LX1033 and the achievement of an investigational new drug application for LX7101, as well as his strategic and operational leadership and participation in business development activities.

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 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. For each of our executive officers, we left base salaries unchanged from the previous year in February 2009, increased base salaries in February 2010 and left base salaries unchanged from the previous year in February 2011 and February 2012. The base salaries of our 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 2009,

2010, 2011 and 2012, 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 2010 with respect to 2009 performance, the compensation committee included the relevant factors described above under “- Corporate and Individual Performance Criteria - February 2010 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 partially achieved, and awarded bonuses for 2009 performance to Dr. Sands and our other executive officers in an amount reflecting such partial achievement.

In determining the cash bonus awards paid in February 2011 with respect to 2010 performance, the compensation committee included the relevant factors described above under “- Corporate and Individual Performance Criteria - February 2011 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 partially achieved, and awarded bonuses for 2010 performance to Dr. Sands and our other executive officers in an amount reflecting such partial achievement. However, in light of prevailing economic conditions and a desire to conserve the company's cash and investment resources, the compensation committee determined that fifty percent of such bonuses would be payable in cash and fifty percent would be payable in stock bonus awards granted under our Equity Incentive Plan.

In determining the cash bonus awards paid in February 2012 with respect to 2011 performance, the compensation committee included the relevant factors described above under “- Corporate and Individual Performance Criteria - February 2012 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 partially achieved, and awarded bonuses for 2011 performance to Dr. Sands and our other executive officers in an amount reflecting such partial achievement.

Long-Term Stock-Based Incentive Awards

All of our employees, including our executive and other officers, are eligible to receive long-term stock-based incentive awards under our 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 Equity Incentive Plan enhances our ability to attract and retain the services of qualified individuals. Factors considered in determining whether and in what amounts such awards are granted to an officer include the executive's position, his performance and responsibilities, the amount of stock options and other stock awards currently held by the officer, the vesting schedules of any such options and stock awards and the officer'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 2009 and 2010, the compensation committee approved annual stock option grants under our Equity Incentive Plan to executive officers and other employees who satisfied eligibility requirements, including time of service. In 2011 and 2012, the compensation committee approved a mix of annual stock option grants and restricted stock unit awards under our Equity Incentive Plan to eligible executive officers and other employees, with stock options comprising a larger portion of such mix for executive 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 biotechnology industry.

In February 2009, the compensation committee determined not to award cash bonuses to our officers with respect to 2008 performance in light of prevailing economic conditions, the state of the financial markets, and a desire to

conserve the company's cash and investment resources. Instead, the compensation committee approved the grant to our officers of restricted stock bonus awards under our Equity Incentive Plan. The amounts of such awards were determined by the compensation committee based on its assessment of the achievement of the corporate and individual goals originally established for purposes of determining 2008 cash bonuses, including the relevant factors described above under “- Corporate and Individual Performance Criteria” in its evaluation of corporate performance. The awarded amounts reflected the compensation committee's determination that our corporate objectives for the year had been partially achieved. Taking into account both the background and nature of the awards and a desire to achieve retention and incentive objectives, the shares subject to the awards were made subject to vesting in two installments over the one-year period following the date of grant.

In February 2010, the compensation committee approved the grant to our officers of restricted stock unit awards under our Equity Incentive Plan. The shares subject to such restricted stock unit awards will vest and become issuable upon the dosing

of the first patient in a pivotal human clinical trial in any country the results of which could be used to establish safety and efficacy of a pharmaceutical product discovered or developed by us (whether or not licensed by us to a third party) as a basis for a New Drug Application with the U.S. Food and Drug Administration or that would otherwise satisfy the requirements of 21 CFR 312.21(c) or its foreign equivalent. The compensation committee decided to create such awards to provide a meaningful equity incentive tied to the achievement of what the committee considered to be a very important milestone in our company's overall development. In determining the amounts of such grants, the compensation committee considered historical individual performance and individual bonus targets, making awards valued in total at approximately one-half of our aggregate officer bonus target pool.

As described above under “- Cash Bonus Awards,” in light of prevailing economic conditions and a desire to conserve the company's cash and investment resources, the compensation committee determined that bonus awards paid in February 2011 with respect to 2010 performance would be payable fifty percent in cash and fifty percent in stock bonus awards granted under our Equity Incentive Plan. Taking into account the nature of such awards as a bonus for 2010 performance, the shares subject to the stock bonus awards were not made subject to vesting conditions.

Summary Compensation Table for 2011

The following table presents summary information regarding the compensation of each of Arthur T. Sands, M.D., Ph.D., 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, 2011. We have entered into employment agreements and other employment arrangements with each of our named executive officers, the material terms of which are described below.

Based on the summary compensation information provided below, “Salary” accounted for approximately 35%, 35% and 36% of the total compensation paid to our named executive officers in 2011, 2010 and 2009, respectively, and “Bonus” accounted for approximately 10%, 3% and 10% of the total compensation paid to our named executive officers for 2011, 2010 and 2009, respectively.

| Name and Position | Year | Salary | Bonus ⁽¹⁾ | Stock Awards ⁽²⁾ | Option Awards ⁽³⁾ | All Other Compensation ⁽⁴⁾ | Total |
|--|------|-----------|----------------------|-----------------------------|------------------------------|---------------------------------------|-------------|
| Arthur T. Sands, M.D., Ph.D. President, Chief Executive Officer and Director | 2011 | \$580,000 | \$195,000 | \$332,450 | \$803,822 | \$6,845 | \$1,918,117 |
| | 2010 | \$577,500 | \$70,000 | \$140,030 | \$1,127,381 | \$6,855 | \$1,921,766 |
| | 2009 | \$560,000 | \$210,000 | \$149,930 | \$841,263 | \$6,965 | \$1,768,158 |
| Jeffrey L. Wade, J.D. Executive Vice President, Corporate Development and Chief Financial Officer | 2011 | \$385,000 | \$105,000 | \$170,750 | \$415,770 | \$6,679 | \$1,083,199 |
| | 2010 | \$374,375 | \$35,000 | \$60,040 | \$670,268 | \$6,668 | \$1,146,351 |
| | 2009 | \$340,000 | \$90,000 | \$64,960 | \$407,063 | \$6,696 | \$908,719 |
| Alan J. Main, Ph.D. Executive Vice President of Pharmaceutical Research | 2011 | \$350,000 | \$80,000 | \$152,650 | \$360,334 | \$6,629 | \$949,613 |
| | 2010 | \$348,750 | \$35,000 | \$60,040 | \$478,953 | \$6,633 | \$929,376 |
| | 2009 | \$340,000 | \$90,000 | \$64,960 | \$352,788 | \$6,696 | \$854,444 |
| Brian P. Zambrowicz, Ph.D. Executive Vice President and Chief Scientific Officer | 2011 | \$400,000 | \$115,000 | \$201,350 | \$471,206 | \$6,701 | \$1,194,257 |
| | 2010 | \$395,625 | \$47,500 | \$79,990 | \$663,165 | \$6,700 | \$1,192,980 |
| | 2009 | \$365,000 | \$120,000 | \$80,040 | \$488,475 | \$6,738 | \$1,060,253 |
| Pablo Lapuerta, M.D. Senior Vice President, Clinical Development and Chief Medical Officer | 2011 | \$268,038 | \$55,000 | — | \$262,820 | \$6,498 | \$592,356 |

(1)

Bonus amounts paid with respect to 2010 performance reflect only cash bonus payments and do not include the aggregate grant date fair value of stock bonus awards granted in February 2011 with respect to 2010 performance. All stock awards reflect the aggregate grant date fair value of such award computed in accordance with FASB ASC Topic 718, 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 Equity Incentive Plan. Stock awards

(2) granted in 2011 reflect restricted stock units granted in February 2011 and stock bonus awards granted in February 2011 with respect to 2010 performance. Stock awards granted in 2010 reflect restricted stock units granted in February 2010. Stock awards granted in 2009 reflect restricted stock bonus awards granted in February 2009 in lieu of 2008 cash bonuses.

Reflects the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of stock options granted in 2011, 2010 and 2009. See the information appearing under the heading entitled “Stock-Based

(3) 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, 2011 for certain assumptions made in the valuation of such stock options.

(4) 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 all employees.

| | Year | Company 401(k) Matching Contribution | Company-Paid Group Term Life Insurance Premiums |
|------------------------------|------|---|--|
| Arthur T. Sands, M.D., Ph.D. | 2011 | \$6,125 | \$720 |
| | 2010 | \$6,125 | \$730 |
| | 2009 | \$6,125 | \$840 |
| Jeffrey L. Wade, J.D. | 2011 | \$6,125 | \$554 |
| | 2010 | \$6,125 | \$543 |
| | 2009 | \$6,125 | \$571 |
| Alan J. Main, Ph.D. | 2011 | \$6,125 | \$504 |
| | 2010 | \$6,125 | \$508 |
| | 2009 | \$6,125 | \$571 |
| Brian P. Zambrowicz, Ph.D. | 2011 | \$6,125 | \$576 |
| | 2010 | \$6,125 | \$575 |
| | 2009 | \$6,125 | \$613 |
| Pablo Lapuerta, M.D. | 2011 | \$6,125 | \$373 |

Employment Agreements and Other Employment Arrangements

In October 1999, we entered into an employment agreement with Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, which was subsequently restated in February 2006. Under the agreement, Dr. Sands receives a base salary, currently \$580,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. 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. Sands' employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

In December 1998, we entered into an employment agreement with Jeffrey L. Wade, J.D. to serve as our senior vice president and chief financial officer starting in January 1999. Mr. Wade was named executive vice president and general counsel in February 2000 and executive vice president, corporate development and chief financial officer in May 2010. Under the agreement, Mr. Wade receives a base salary, currently \$385,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. 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."

In July 2001, we entered into an employment agreement with Alan J. Main, Ph.D., then our senior vice president, Lexicon Pharmaceuticals. In February 2007, Dr. Main was named executive vice president of pharmaceutical research. Under the agreement, Dr. Main receives a base salary, currently \$350,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. 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."

In February 2000, we entered into an employment agreement with Brian P. Zambrowicz, Ph.D., then our senior vice president of genomics. Dr. Zambrowicz was named executive vice president of research in August 2002 and executive vice president and chief scientific officer in February 2007. Under the agreement, Dr. Zambrowicz receives a base salary, currently \$400,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. 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.

Zambrowicz's employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

In March 2011, we entered into an offer letter with Pablo Lapuerta, M.D. to serve as our senior vice president, clinical development and chief medical officer. Under the offer letter, Dr. Lapuerta receives a base salary, currently \$345,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The offer letter provides for certain severance payments upon the termination of Dr. Lapuerta's employment, as described below under the heading "Executive and Director Compensation - Potential Payments upon Termination or Change in Control."

Grants of Plan-Based Awards in 2011

The following table presents each grant of stock bonus awards, restricted stock units and stock options in 2011 to the individuals named in the summary compensation table.

| Name | Grant Date | Number of Stock Bonus Awards | Number of Restricted Stock Units | Number of Securities Underlying Options | Exercise Price of Option Awards | Grant Date Fair Value of Stock and Option Awards |
|------------------------------|------------|------------------------------|----------------------------------|---|---------------------------------|--|
| Arthur T. Sands, M.D., Ph.D. | 2/23/2011 | 38,674 | | | | \$70,000 |
| | 2/23/2011 | | 145,000 | | | \$262,450 |
| | 2/23/2011 | | | 580,000 | \$ 1.81 | \$803,822 |
| Jeffrey L. Wade, J.D. | 2/23/2011 | 19,337 | | | | \$35,000 |
| | 2/23/2011 | | 75,000 | | | \$135,750 |
| | 2/23/2011 | | | 300,000 | \$ 1.81 | \$415,770 |
| Alan J. Main, Ph.D. | 2/23/2011 | 19,337 | | | | \$35,000 |
| | 2/23/2011 | | 65,000 | | | \$117,650 |
| | 2/23/2011 | | | 260,000 | \$ 1.81 | \$360,334 |
| Brian P. Zambrowicz, Ph.D. | 2/23/2011 | 26,243 | | | | \$47,500 |
| | 2/23/2011 | | 85,000 | | | \$153,850 |
| | 2/23/2011 | | | 340,000 | \$ 1.81 | \$471,206 |
| Pablo Lapuerta, M.D. | 3/23/2011 | | | 200,000 | \$ 1.72 | \$262,820 |

Each of the stock bonus awards in the foregoing table was granted under our Equity Incentive Plan and was not subject to vesting conditions.

Each of the restricted stock units in the foregoing table was granted under our Equity Incentive Plan. Each restricted stock unit vests with respect to 25% of the shares underlying the restricted stock unit on February 28, 2012 and with respect to an additional 25% of the shares underlying the restricted stock unit on February 28 of each of the three 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 following a change in control of our company.

Each of the options in the foregoing table was granted under our 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 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 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, 2011

The following table presents information about unexercised options and unvested restricted stock units that were held by each of the individuals listed in the summary compensation table as of December 31, 2011.

| | 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 | Market Value of Restricted Stock Units That Have Not Vested |
| | Exercisable | Unexercisable (1) | | | | (4) |
| Arthur T. Sands, M.D., Ph.D. | 170,000 | — | \$9.38 | 2/19/2012 | | |
| | 135,000 | — | \$3.90 | 2/14/2013 | | |
| | 150,000 | — | \$7.59 | 2/12/2014 | | |
| | 150,000 | — | \$5.76 | 2/18/2015 | | |
| | 380,000 | — | \$4.00 | 2/1/2016 | | |
| | 340,000 | — | \$3.94 | 2/13/2017 | | |
| | 551,172 | 23,828 | \$2.07 | 2/7/2018 | | |
| | 549,072 | 225,928 | \$1.45 | 2/12/2019 | | |
| | 350,676 | 414,324 | \$1.90 | 2/15/2020 | | |
| | — | 580,000 | \$1.81 | 2/23/2021 | | |
| | | | | | 73,700 (2) | \$ 95,073 |
| | | | | | 145,000 (3) | \$ 187,050 |
| Jeffrey L. Wade, J.D. | 65,000 | — | \$9.38 | 2/19/2012 | | |
| | 54,000 | — | \$3.90 | 2/14/2013 | | |
| | 60,000 | — | \$7.59 | 2/12/2014 | | |
| | 60,000 | — | \$5.76 | 2/18/2015 | | |
| | 120,000 | — | \$4.00 | 2/1/2016 | | |
| | 120,000 | — | \$3.94 | 2/13/2017 | | |
| | 191,712 | 8,288 | \$2.07 | 2/7/2018 | | |
| | 265,680 | 109,320 | \$1.45 | 2/12/2019 | | |
| | 171,900 | 203,100 | \$1.90 | 2/15/2020 | | |
| | 39,588 | 60,412 | \$1.52 | 5/17/2020 | | |
| | — | 300,000 | \$1.81 | 2/23/2021 | | |
| | | | | | 31,600 (2) | \$ 40,764 |
| | | | | | 75,000 (3) | \$ 96,750 |
| Alan J. Main, Ph.D. | 15,000 | — | \$9.38 | 2/19/2012 | | |
| | 54,000 | — | \$3.90 | 2/14/2013 | | |
| | 50,000 | — | \$7.59 | 2/12/2014 | | |
| | 50,000 | — | \$5.76 | 2/18/2015 | | |
| | 65,000 | — | \$4.00 | 2/1/2016 | | |
| | 100,000 | — | \$3.94 | 2/13/2017 | | |
| | 191,712 | 8,288 | \$2.07 | 2/7/2018 | | |
| | 230,256 | 94,744 | \$1.45 | 2/12/2019 | | |
| | 148,980 | 176,020 | \$1.90 | 2/15/2020 | | |
| | — | 260,000 | \$1.81 | 2/23/2021 | | |

| | |
|-----------------------|-----------|
| 31,600 ⁽²⁾ | \$ 40,764 |
| 65,000 ⁽³⁾ | \$ 83,850 |

| | | | | | | |
|----------------------------|---------|---------|--------|-----------|-----------------------|------------|
| Brian P. Zambrowicz, Ph.D. | 75,000 | — | \$9.38 | 2/19/2012 | | |
| | 63,000 | — | \$3.90 | 2/14/2013 | | |
| | 70,000 | — | \$7.59 | 2/12/2014 | | |
| | 70,000 | — | \$5.76 | 2/18/2015 | | |
| | 170,000 | — | \$4.00 | 2/1/2016 | | |
| | 200,000 | — | \$3.94 | 2/13/2017 | | |
| | 359,460 | 15,540 | \$2.07 | 2/7/2018 | | |
| | 318,816 | 131,184 | \$1.45 | 2/12/2019 | | |
| | 206,280 | 243,720 | \$1.90 | 2/15/2020 | | |
| | — | 340,000 | \$1.81 | 2/23/2021 | | |
| | | | | | 42,100 ⁽²⁾ | \$ 54,309 |
| | | | | | 85,000 ⁽³⁾ | \$ 109,650 |
| Pablo Lapuerta, M.D. | — | 200,000 | \$1.72 | 3/23/2021 | | |

(1) 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 restricted stock unit vests upon the dosing of the first patient in a pivotal human clinical trial in any country the results of which could be used to establish safety and efficacy of a pharmaceutical product we discovered or

(2) developed (whether or not licensed by us to a third party) as a basis for a New Drug Application with the U.S. Food and Drug Administration or that would otherwise satisfy the requirements of 21 CFR 312.21(c) or its foreign equivalent.

(3) Each restricted stock unit vests with respect to 25% of the shares underlying the restricted stock unit on February 28, 2012 and with respect to an additional 25% of the shares underlying the restricted stock unit on February 28 of each of the three following years.

(4) Based on the closing price of our common stock on the Nasdaq Global Select Market of \$1.29 per share on December 30, 2011.

Potential Payments upon Termination or Change in Control

Employment Agreements

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

Under our employment agreement with Dr. Sands, “good reason” means any of the following, without Dr. Sands' prior written consent:

- any material diminution in Dr. Sands' base compensation, followed by Dr. Sands terminating his employment for “good reason” within 120 days after receiving notice of such diminution;

- any material diminution in Dr. Sands' authority, duties or responsibilities, followed by Dr. Sands terminating his employment for “good reason” within 120 days after receiving notice of such diminution;

- any requirement that Dr. Sands report to an officer or other employee of our company rather than reporting directly to our board of directors, followed by Dr. Sands terminating his employment for “good reason” within 120 days after receiving notice of such requirement; or

- any material breach by our company of the agreement, followed by Dr. Sands terminating his employment for “good reason” within 120 days after receiving notice of such breach.

Jeffrey L. Wade, J.D. 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. Under our employment agreement with Mr. Wade, “good reason” means any of the following, without Mr. Wade's prior written consent:

37

any material diminution in Mr. Wade's base compensation, followed by Mr. Wade terminating his employment for "good reason" within 120 days after receiving notice of such diminution;

- any material diminution in Mr. Wade's authority, duties or responsibilities, followed by Mr. Wade 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 Mr. Wade terminating his employment for "good reason" within 120 days after receiving notice of such breach.

Alan J. Main, Ph.D. 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 our employment agreement with Dr. Main, "good reason" means any of the following, without Dr. Main's prior written consent:

- any material diminution in Dr. Main's base compensation, followed by Dr. Main terminating his employment for "good reason" within 120 days after receiving notice of such diminution;

- any material diminution in Dr. Main's authority, duties or responsibilities, followed by Dr. Main 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 Dr. Main terminating his employment for "good reason" within 120 days after receiving notice of such breach.

Brian P. Zambrowicz, Ph.D. Our employment agreement with Dr. Zambrowicz provides that if we terminate his employment without "cause" or if Dr. Zambrowicz terminates his employment for "good reason," we will pay Dr. Zambrowicz 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. Zambrowicz his then-current salary for six months pursuant to our normal payroll procedures.

Under our employment agreement with Dr. Zambrowicz, "good reason" means any of the following, without Dr. Zambrowicz's prior written consent:

- any material diminution in Dr. Zambrowicz's base compensation, followed by Dr. Zambrowicz terminating his employment for "good reason" within 120 days after receiving notice of such diminution;

- any material diminution in Dr. Zambrowicz's authority, duties or responsibilities, followed by Dr. Zambrowicz 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 Dr. Zambrowicz terminating his employment for "good reason" within 120 days after receiving notice of such breach.

Under each of our employment agreements with the individuals named in the summary compensation table, "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 in a court of competent jurisdiction of a felony; or

- a breach by the individual during his or her 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.

Other Employment Arrangements

Pablo Lapuerta, M.D. Our offer letter with Dr. Lapuerta provides that if we terminate his employment without “cause,” we would pay Dr. Lapuerta his then-current salary for six months pursuant to our normal payroll procedures. Such payments would be extended to twelve months if Dr. Lapuerta's employment were terminated without “cause” in connection with a “change in control.” Under our offer letter with Dr. Lapuerta, “cause” means any of the following:

- Dr. Lapuerta having engaged in intentional misconduct causing our material violation of any state or federal laws;
- Dr. Lapuerta 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 Dr. Lapuerta that was intended to result in personal enrichment of Dr. Lapuerta at our expense; or
- Dr. Lapuerta's conviction of a felony.

Under our offer letter with Dr. Lapuerta, 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.

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;
- 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;
- 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, however, a change in control shall not have occurred as a result of the consummation of any of the transactions contemplated by our securities purchase agreement and stockholders' agreement with Invus, L.P., including the completion of a pro rata rights offering to our stockholders in December 2011 which resulted in Invus and its affiliates becoming the beneficial owner of more than 50% of the outstanding shares of our common stock.

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;

- 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;

- 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, "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, however, a change in control shall not have occurred as a result of the consummation of any of the transactions contemplated by our securities purchase agreement and stockholders' agreement with Invus, L.P., including the completion of a pro rata rights offering to our stockholders in December 2011 which resulted in Invus and its affiliates becoming the beneficial owner of more than 50% of the outstanding shares of our common stock.

Under the restricted stock unit agreements, "good reason" means any of the following, without the named executive officer'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, 2011. 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 ⁽⁶⁾ | Accelerated Portion of Stock Options ⁽⁷⁾ | Accelerated Portion of Restricted Stock Units ⁽⁸⁾ |
|------------------------------|-------------------------------|----------------------|---|--|
| Arthur T. Sands, M.D., Ph.D. | \$580,000 ⁽¹⁾ | \$290,000 | — | \$282,123 |
| Jeffrey L. Wade, J.D. | \$385,000 ⁽²⁾ | \$77,000 | — | \$137,514 |
| Alan J. Main, Ph.D. | \$350,000 ⁽³⁾ | \$61,250 | — | \$124,614 |
| Brian P. Zambrowicz, Ph.D. | \$400,000 ⁽⁴⁾ | \$80,000 | — | \$163,959 |
| Pablo Lapuerta, M.D. | \$345,000 ⁽⁵⁾ | — | — | — |

Reflects aggregate salary continuation payments due as a result of our termination of Dr. Sands' employment
⁽¹⁾ without "cause," Dr. Sands' termination of his employment for "good reason," or the termination of Dr. Sands' employment at the end of a renewal term through notice of non-renewal.

Reflects aggregate salary continuation payments due as a result of our termination of Mr. Wade's employment
⁽²⁾ 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 \$182,500.

Reflects aggregate salary continuation payments due as a result of our termination of Dr. Main's employment
⁽³⁾ 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 \$175,000.

Reflects aggregate salary continuation payments due as a result of our termination of Dr. Zambrowicz's
⁽⁴⁾ employment without "cause" or Dr. Zambrowicz's termination of his employment for "good reason." If Dr. Zambrowicz's employment had been terminated at the end of a renewal term through notice of non-renewal, the aggregate salary continuation payment for Dr. Zambrowicz would have been \$200,000.

Reflects aggregate salary continuation payments due as a result of our termination of Dr. Lapuerta's employment
⁽⁵⁾ without "cause" in connection with a "change in control." If Dr. Lapuerta's employment had been terminated without "cause" other than in connection with a "change in control," the aggregate salary continuation payment for Dr. Lapuerta would have been \$172,500.

Reflects single-sum bonus payments due as a result of our termination of the named individual's employment
⁽⁶⁾ without "cause," the named individual's termination of his or her employment for "good reason," or in the case of Dr. Sands, the termination of his employment at the end of a renewal term through notice of non-renewal.

Based on the closing price of our common stock on the Nasdaq Global Select Market on December 31, 2011 of
⁽⁷⁾ \$1.29 per share, less the exercise price payable with respect to the stock options for which vesting would have been accelerated.

Based on the closing price of our common stock on the Nasdaq Global Select Market on December 31, 2011 of
⁽⁸⁾ \$1.29 per share.

Director Compensation in 2011

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

- an annual retainer of \$15,000 for service on the board of directors (\$30,000 for service as non-executive chairman of the board of directors), prorated for any partial year of service;

- an annual retainer of \$2,500 for service on each committee of the board of directors of which he or she is a member (\$5,000 for service as chairman of any such committee), prorated for any partial year of service;

- a fee of \$2,500 for each meeting of the board of directors that he or she attends in person (\$500 for each telephonic meeting of the board of directors in which he or she participates); and

- a fee of \$1,000 for each committee meeting that he or she attends in person other than in connection with a meeting of the full board of directors (\$500 for each telephonic committee meeting in which he or she participates).

Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, does not receive additional compensation for his service as a director. We make additional cash payments to Dr. Lefkowitz for his consulting services and to Dr. Nies for his consulting services as chairman of our medical advisory board.

Our Non-Employee Directors' Stock Option Plan currently provides for the grant of options to purchase shares of common stock to our non-employee directors. All non-employee directors receive an initial option to purchase 30,000 shares of common stock. In addition, all non-employee directors who have served in such capacity for six months currently receive an annual option to purchase 10,000 shares of common stock (or 20,000 shares, in the case of the non-employee chairman of our board of directors). All options granted under the non-employee directors' plan have an exercise price equal to the fair market value of our common stock on the date of grant.

The following table presents summary information for the year ended December 31, 2011 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) | All Other Compensation | Total |
|---------------------------|-----------------------------|---|---------------------------|-----------|
| Raymond Debbane | \$31,500 | \$12,912 | — | \$44,412 |
| Philippe J. Amouyal | \$31,000 | \$12,912 | — | \$43,912 |
| Samuel L. Barker, Ph.D. | \$47,500 | \$25,824 | — | \$73,324 |
| Robert J. Lefkowitz, M.D. | \$28,500 | \$12,912 | \$ 50,000 ⁽⁴⁾ | \$91,412 |
| Alan S. Nies, M.D. | \$31,000 | \$12,912 | \$ 115,000 ⁽⁵⁾ | \$158,912 |
| Frank P. Palantoni | \$36,500 | \$12,912 | — | \$49,412 |
| Christopher J. Sobecki | \$26,500 | \$12,912 | — | \$39,412 |
| Judith L. Swain, M.D. | \$32,000 | \$12,912 | — | \$44,912 |

Reflects the aggregate grant date fair value, computed in accordance with FASB ASC Topic 718, of stock options granted in 2011. 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, 2011 for certain assumptions made in the valuation of such stock options.

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

| Name | Number of Securities Underlying Unexercised Options |
|---------------------------|---|
| Raymond Debbane | 70,000 |
| Philippe J. Amouyal | 70,000 |
| Samuel L. Barker, Ph.D. | 158,000 |
| Robert J. Lefkowitz, M.D. | 88,000 |
| Alan S. Nies, M.D. | 108,500 |
| Frank P. Palantoni | 90,000 |
| Christopher J. Sobecki | 70,000 |
| Judith L. Swain, M.D. | 70,000 |

⁽³⁾ The following table presents the fair value of each grant of stock options in 2011 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 | Grant Date Fair Value of Options |
|---------------------------|------------|---|---------------------------------|----------------------------------|
| Raymond Debbane | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |
| Philippe Amouyal | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |
| Samuel L. Barker, Ph.D. | 4/29/2011 | 20,000 | \$ 1.69 | \$25,824 |
| Robert J. Lefkowitz, M.D. | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |
| Alan S. Nies, M.D. | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |
| Frank P. Palantoni | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |
| Christopher J. Sobecki | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |
| Judith L. Swain, M.D. | 4/29/2011 | 10,000 | \$ 1.69 | \$12,912 |

⁽⁴⁾ Consists of amounts paid to Dr. Lefkowitz for his consulting services.

⁽⁵⁾ Consists of amounts paid to Dr. Nies for his consulting services as chairman of our medical advisory board.

Compensation Committee Report

The compensation committee of our board of directors is responsible for evaluating the performance of management, determining the compensation of our executive and other officers and administering our Equity Incentive Plan, under which stock option grants and other stock awards may be made to our employees.

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, 2011.

Compensation Committee

Frank P. Palantoni (chair)

Philippe J. Amouyal

Alan S. Nies, M.D.

42

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 November __, 2012. Any such proposal must also comply with Securities and Exchange Commission regulations regarding the inclusion of stockholder proposals in company-sponsored proxy materials. 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 November __, 2012. You may contact the 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., 8800 Technology Forest Place, The Woodlands, Texas 77381.

By order of the board of directors,

Brian T. Crum
Secretary

March __, 2012
The Woodlands, Texas

Appendix A

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."

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 May 6, 1998. A

SECOND: Restated Certificate of Incorporation of the Corporation was filed in the Office of the Secretary of State on April 5, 2000 and was subsequently amended by Certificates of Amendment to the Restated Certificate of Incorporation filed in the Office of the Secretary of State on April 25, 2007, August 23, 2007 and July 15, 2009.

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 Amended and Restated Certificate of Incorporation (including the

THIRD: amendments to the Corporation's Certificate of Incorporation effected hereby) and (ii) proposed that the Corporation's stockholders adopt and approve this Amended and Restated Certificate of Incorporation (including the amendments to the Corporation's Certificate of Incorporation effected hereby).

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 Section 228 of the DGCL, approved and adopted on behalf of the stockholders this Amended and Restated Certificate of

FOURTH: Incorporation (including the amendments to the Corporation's Certificate of Incorporation effected hereby).

All designations of series of preferred stock pursuant to the Certificate of Designations of Series A Cumulative Preferred Stock shall continue to be integrated into this Amended and Restated Certificate of Incorporation until eliminated by the Board of Directors in accordance with Section 151(g) of the DGCL.

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

SIXTH: The Restated Certificate of Incorporation of the Corporation, as amended, 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 905,000,000 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) 900,000,000 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) 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;

A -2

(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

A -3

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

A -4

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.

A -5

(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

A -6

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.

A -7

IN WITNESS WHEREOF, this 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 April ____, 2012.

LEXICON PHARMACEUTICALS, INC.

By:
Arthur T. Sands
President and Chief Executive Officer

Attest:

By:
Brian T. Crum
Secretary

A -8

Appendix B

LEXICON PHARMACEUTICALS, INC.

EQUITY INCENTIVE PLAN

This Plan initially was established as the Lexicon Genetics Incorporated 1995 Stock Option Plan (the “1995 Stock Option Plan”), which was adopted by the Board and approved by the Company's stockholders on September 13, 1995. The 1995 Stock Option Plan was subsequently amended and restated in its entirety and renamed the Lexicon Genetics Incorporated 2000 Equity Incentive Plan (the “2000 Equity Incentive Plan”), which was adopted by the Board on February 3, 2000 and approved by the Company's stockholders on March 15, 2000 and May 19, 2004. The 2000 Equity Incentive Plan was subsequently amended and restated in its entirety and renamed the Equity Incentive Plan, which was adopted by the Board on February 27, 2009 and approved by the Company's stockholders on April 23, 2009. A subsequent amendment to the Equity Incentive Plan was approved by the Board on February 16, 2012 subject to approval by the Company's stockholders. The terms of this Plan shall supersede the terms of the 1995 Stock Option Plan and the 2000 Equity Incentive Plan in their entirety; provided, however, that nothing herein shall operate or be construed as modifying the terms of an Incentive Stock Option granted under the 1995 Stock Option Plan or the 2000 Equity Incentive Plan in a manner that would treat the option as being a new grant for purpose of Section 424(h) of the Code.

1. PURPOSES.

(a) ELIGIBLE STOCK AWARD RECIPIENTS. The persons eligible to receive Stock Awards are the Employees, Directors and Consultants of the Company and its Affiliates.

(b) AVAILABLE STOCK AWARDS. The purpose of the Plan is to provide a means by which eligible recipients of Stock Awards may be given an opportunity to benefit from increases in value of the Common Stock through the granting of the following Stock Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) Stock Bonus Awards, (iv) Restricted Stock Awards, (v) Phantom Stock Awards and (vi) Stock Appreciation Rights.

(c) GENERAL PURPOSE. The Company, by means of the Plan, seeks to retain the services of the group of persons eligible to receive Stock Awards, to secure and retain the services of new members of this group and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Affiliates.

2. DEFINITIONS.

(a) “AFFILIATE” means any parent corporation or subsidiary corporation of the Company, whether now or hereafter existing, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.

(b) “BOARD” means the Board of Directors of the Company.

(c) “CODE” means the Internal Revenue Code of 1986, as amended.

(d) “COMMITTEE” means a committee of one or more members of the Board appointed by the Board in accordance with subsection 3(c).

(e) “COMMON STOCK” means the common stock, par value \$.001 per share, of the Company.

(f) “COMPANY” means Lexicon Pharmaceuticals, Inc. a Delaware corporation.

(g) “CONSULTANT” means any person other than a Director or Employee who is engaged by the Company or an Affiliate to render consulting or advisory services and who is compensated for such services.

(h) “CONTINUOUS SERVICE” means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. The Participant's Continuous Service shall not be deemed to have terminated merely because of a change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's Continuous Service. For example, a change in status from an Employee of the Company to a Consultant of an Affiliate or a Director will not constitute an interruption of Continuous Service. The Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave.

B -1

- (i)“COVERED EMPLOYEE” means the chief executive officer and the four (4) other highest compensated officers of the Company for whom total compensation is required to be reported to stockholders under the Exchange Act, as determined for purposes of Section 162(m) of the Code.
- (j)“DIRECTOR” means a member of the Board of Directors of the Company.
- (k)“DISABILITY” means the permanent and total disability of a person within the meaning of Section 22(e)(3) of the Code.
- (l)“EMPLOYEE” means any person (which may include a Director) who is employed by the Company or an Affiliate.
- (m)“EXCHANGE ACT” means the Securities Exchange Act of 1934, as amended.
- (n)“FAIR MARKET VALUE” means, as of any date, the value of the Common Stock determined as follows:
- (i)If the Common Stock is listed on any established stock exchange or traded on the Nasdaq Stock Market, the Fair Market Value of a share of Common Stock shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the last market trading day prior to the day of determination, as reported in The Wall Street Journal or such other source as the Board deems reliable.
- (ii)In the absence of such markets for the Common Stock, the Fair Market Value shall be determined in good faith by the Board in such manner as it deems appropriate and as is consistent with the requirements of section 409A of the Code.
- (o)“INCENTIVE STOCK OPTION” means an option to purchase Common Stock that is intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.
- (p)“NON-EMPLOYEE DIRECTOR” means a Director who either (i) is not a current Employee or Officer of the Company or its parent or a subsidiary, does not receive compensation (directly or indirectly) from the Company or its parent for a subsidiary for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act (“Regulation S-K”)), does not possess an interest in any other transaction as to which disclosure would be required under Item 404(a) of Regulation S-K and is not engaged in a business relationship as to which disclosure would be required under Item 404(b) of Regulation S-K; or (ii) is otherwise considered a “non-employee director” for purposes of Rule 16b-3.
- (q)“NONSTATUTORY STOCK OPTION” means an option to purchase Common Stock other than an Incentive Stock Option.
- (r)“OFFICER” means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act and the rules and regulations promulgated thereunder.
- (s)“OPTION” means an Incentive Stock Option or a Nonstatutory Stock Option granted pursuant to Section 6 of the Plan.
- (t)“OPTION AGREEMENT” means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an individual Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.
- (u)“OPTIONHOLDER” means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.
- (v)“OUTSIDE DIRECTOR” means a Director who either (i) is not a current employee of the Company or an “affiliated corporation” (within the meaning of Treasury Regulations promulgated under Section 162(m) of the Code), is not a former employee of the Company or an “affiliated corporation” receiving compensation for prior services (other than benefits under a tax qualified pension plan), was not an officer of the Company or an “affiliated corporation” at any time and is not currently receiving direct or indirect remuneration from the Company or an “affiliated corporation” for services in any capacity other than as a Director or (ii) is otherwise considered an “outside director” for purposes of Section 162(m) of the Code.
- (w)“PARTICIPANT” means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

- (x)“PHANTOM STOCK AWARD” means a right to receive shares of Common Stock (or the Fair Market Value thereof) granted pursuant to Section 7(c) of the Plan.
- (y)“PLAN” means this Lexicon Pharmaceuticals, Inc. Equity Incentive Plan.
- (z)“RESTRICTED STOCK AWARD” means a right to purchase restricted Common Stock granted pursuant to Section 7(b) of the Plan.
- (aa)“RULE 16B-3” means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b 3, as in effect from time to time.
- (ab)“SECURITIES ACT” means the Securities Act of 1933, as amended.
- (ac)“STOCK APPRECIATION RIGHT” means a right to receive an amount equal to any appreciation or increase in the Fair Market Value of Common Stock over a specified period of time granted pursuant to Section 7(d) of the Plan.
- (ad)“STOCK AWARD” means any right granted under the Plan, including an Option, a Stock Bonus Award, a Restricted Stock Award, a Phantom Stock Award, or a Stock Appreciation Right.
- (ae)“STOCK AWARD AGREEMENT” means a written agreement between the Company and a holder of a Stock Award evidencing the terms and conditions of an individual Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.
- (af)“STOCK BONUS AWARD” means an award of Common Stock granted pursuant to Section 7(a) of the Plan.
- (ag)“TEN PERCENT STOCKHOLDER” means a person who owns (or is deemed to own pursuant to Section 424(d) of the Code) stock possessing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or of any of its Affiliates.

3. ADMINISTRATION.

- (a)ADMINISTRATION BY BOARD. The Board shall administer the Plan unless and until the Board delegates administration to a Committee, as provided in subsection 3(c).
- (b)POWERS OF BOARD. The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:
- (i)To determine from time to time which of the persons eligible under the Plan shall be granted Stock Awards; when and how each Stock Award shall be granted; what type or combination of types of Stock Award shall be granted; the provisions of each Stock Award granted (which need not be identical), including the time or times when a person shall be permitted to receive Common Stock pursuant to a Stock Award; and the number of shares of Common Stock with respect to which a Stock Award shall be granted to each such person.
- (ii)To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.
- (iii)To amend the Plan or a Stock Award as provided in Section 12.
- (iv)To terminate or suspend the Plan as provided in Section 13.
- (v)Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company that are not in conflict with the provisions of the Plan.
- (c)DELEGATION TO COMMITTEE.
- (i)GENERAL. The Board may delegate administration of the Plan to a Committee or Committees of one (1) or more members of the Board, and the term “Committee” shall apply to any person or persons to whom such authority has been delegated. If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent

with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revest in the Board the administration of the Plan.

(ii) **COMMITTEE COMPOSITION WHEN COMMON STOCK IS PUBLICLY TRADED.** At such time as the Common Stock is publicly traded, in the discretion of the Board, a Committee may consist solely of two or more Outside Directors, in accordance with Section 162(m) of the Code, and/or solely of two or more Non-Employee Directors, in accordance with Rule 16b-3. Within the scope of such authority, the Board or the Committee may (A) delegate to a committee of one or more members of the Board who are not Outside Directors the authority to grant Stock Awards to eligible persons who are either (1) not then Covered Employees and are not expected to be Covered Employees at the time of recognition of income resulting from such Stock Award or (2) not persons with respect to whom the Company wishes to comply with Section 162(m) of the Code, and/or (B) delegate to a committee of one or more members of the Board who are not Non-Employee Directors the authority to grant Stock Awards to eligible persons who are not then subject to Section 16 of the Exchange Act.

(d) **EFFECT OF BOARD'S DECISION.** All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

4. SHARES SUBJECT TO THE PLAN.

(a) **SHARE RESERVE.** Subject to the provisions of Section 11 relating to adjustments upon changes in Common Stock, the Common Stock that may be issued pursuant to Stock Awards shall not exceed in the aggregate fifty million (50,000,000) shares.

(b) **REVERSION OF SHARES TO THE SHARE RESERVE.** If any Stock Award shall for any reason expire or otherwise terminate, in whole or in part, without having been exercised in full or shares of Common Stock issued to a Participant pursuant to a Stock Award are forfeited to or repurchased by the Company, including any repurchase or forfeiture caused by the failure to meet a contingency or condition required for the vesting of such shares, the shares of Common Stock not issued under such Stock Award or forfeited to or repurchased by the Company shall revert to and again become available for issuance under the Plan; provided, however, that shares subject to a Stock Award that are not delivered to a Participant because (i) such Participant's right to purchase such shares subject to an Option are surrendered in payment of the exercise price for other shares subject to such Option in a "net exercise," or (ii) such shares are withheld in satisfaction of the withholding of taxes incurred in connection with the exercise of an Option or Stock Appreciation Right, or the issuance of shares under a Stock Bonus Award, Restricted Stock Award or Phantom Stock Award, the shares so surrendered or withheld shall not remain available for subsequent issuance under the Plan.

(c) **SOURCE OF SHARES.** The shares of Common Stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

(d) **SHARES AVAILABLE FOR SPECIFIC STOCK AWARDS.** Subject to the provisions of Section 11 relating to adjustments upon changes in the shares of Common Stock, the Common Stock that may be issued pursuant to Stock Awards other than Options and Stock Appreciation Rights shall not exceed in the aggregate fifteen million (15,000,000) shares.

5. ELIGIBILITY.

(a) **ELIGIBILITY FOR SPECIFIC STOCK AWARDS.** Incentive Stock Options may be granted only to Employees. Stock Awards other than Incentive Stock Options may be granted to Employees, Directors and Consultants.

(b) **TEN PERCENT STOCKHOLDERS.** A Ten Percent Stockholder shall not be granted an Incentive Stock Option unless the exercise price of such Option is at least one hundred ten percent (110%) of the Fair Market Value of the Common Stock at the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

(c) **SECTION 162(m) LIMITATION.** Subject to the provisions of Section 11 relating to adjustments upon changes in the shares of Common Stock, no Employee shall be eligible to be granted Options covering more than three million (3,000,000) shares during any calendar year.

6. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. All Options shall be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates will be issued for shares of Common Stock purchased on exercise of each type of Option. The provisions of separate Options need not be identical, but each

Option shall include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

B -4

- (a)TERM. Subject to the provisions of subsection 5(b) regarding Ten Percent Stockholders, no Option shall be exercisable after the expiration of ten (10) years from the date it was granted.
- (b)EXERCISE PRICE. Subject to the provisions of subsection 5(b) regarding Ten Percent Stockholders, the exercise price of each Option shall be not less than one hundred percent (100%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.
- (c)CONSIDERATION. The purchase price of Common Stock acquired pursuant to an Option shall be paid, to the extent permitted by applicable statutes and regulations, either (i) in cash at the time the Option is exercised or (ii) at the discretion of the Board (1) by delivery to the Company of other Common Stock, (2) according to a deferred payment or other similar arrangement with the Optionholder, (3) by surrender of Optionholder's right to purchase shares subject to an Option (valued, for such purposes, as the Fair Market Value of such surrendered shares on the date of exercise less the exercise price for such surrendered shares) in payment of the exercise price for other shares subject to such Option in a "net exercise" of such Option, or (4) in any other form of legal consideration that may be acceptable to the Board. At any time that the Company is incorporated in Delaware, payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment. In the case of any deferred payment arrangement, interest shall be compounded at least annually and shall be charged at the minimum rate of interest necessary to avoid the treatment as interest, under any applicable provisions of the Code, of any amounts other than amounts stated to be interest under the deferred payment arrangement.
- (d)TRANSFERABILITY. An Incentive Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. A Nonstatutory Stock Option shall be transferable to the extent provided in the Option Agreement; provided that, if the Nonstatutory Stock Option does not provide for transferability, then the Nonstatutory Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.
- (e)VESTING GENERALLY. The total number of shares of Common Stock subject to an Option may, but need not, vest and therefore become exercisable in periodic installments that may, but need not, be equal. The Option may be subject to such other terms and conditions on the time or times when it may be exercised (which may be based on performance or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary.
- (f)TERMINATION OF CONTINUOUS SERVICE. In the event an Optionholder's Continuous Service terminates (other than upon the Optionholder's death or Disability), the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Optionholder's Continuous Service (or such longer or shorter period specified in the Option Agreement), or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified in the Option Agreement, the Option shall terminate.
- (g)EXTENSION OF TERMINATION DATE. An Optionholder's Option Agreement may also provide that if the exercise of the Option following the termination of the Optionholder's Continuous Service (other than upon the Optionholder's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option shall terminate on the earlier of (i) the expiration of the term of the Option set forth in subsection 6(a) or (ii) the expiration of a period of three (3) months after the termination of the Optionholder's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements.
- (h)DISABILITY OF OPTIONHOLDER. In the event that an Optionholder's Continuous Service terminates as a result of the Optionholder's Disability, the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination (or such longer or shorter period specified in the

Option Agreement,) or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified herein, the Option shall terminate.

(i)DEATH OF OPTIONHOLDER. In the event (i) an Optionholder's Continuous Service terminates as a result of the Optionholder's death or (ii) the Optionholder dies within the period (if any) specified in the Option Agreement after the termination of the Optionholder's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Optionholder was entitled to exercise such Option as of the date of death) by the Optionholder's estate, by a person who acquired

B -5

the right to exercise the Option by bequest or inheritance or by a person designated to exercise the Option upon the Optionholder's death pursuant to subsection 6(d), but only within the period ending on the earlier of (1) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Option Agreement) or (2) the expiration of the term of such Option as set forth in the Option Agreement. If, after death, the Option is not exercised within the time specified herein, the Option shall terminate.

7. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS.

(a) STOCK BONUS AWARDS. Each Stock Bonus Award agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of Stock Bonus Award agreements may change from time to time, and the terms and conditions of separate Stock Bonus Award agreements need not be identical, but each Stock Bonus Award agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) CONSIDERATION. A Stock Bonus Award may be granted in consideration for past services actually rendered to the Company or an Affiliate for its benefit.

(ii) VESTING. Shares of Common Stock awarded under the Stock Bonus Award agreement may, but need not, be subject to a share repurchase option or forfeiture restrictions in favor of the Company in accordance with a vesting schedule to be determined by the Board.

(iii) TERMINATION OF PARTICIPANT'S CONTINUOUS SERVICE. In the event a Participant's Continuous Service terminates, the Company may reacquire any or all of the shares of Common Stock held by the Participant which have not vested as of the date of termination under the terms of the Stock Bonus Award agreement.

(iv) TRANSFERABILITY. Rights to acquire shares of Common Stock under the Stock Bonus Award agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the Stock Bonus Award agreement, as the Board shall determine in its discretion, so long as Common Stock awarded under the Stock Bonus Award agreement remains subject to the terms of the Stock Bonus Award agreement.

(b) RESTRICTED STOCK AWARDS. Each Restricted Stock Award agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of the Restricted Stock Award agreement may change from time to time, and the terms and conditions of separate Restricted Stock Award agreements need not be identical, but each Restricted Stock Award agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) PURCHASE PRICE. The purchase price under each Restricted Stock Award agreement shall be such amount as the Board shall determine and designate in such Restricted Stock Award agreement. Such purchase price shall not be less than eighty-five percent (85%) of the Common Stock's Fair Market Value on the date such award is made or at the time the purchase is consummated.

(ii) CONSIDERATION. The purchase price of Common Stock acquired pursuant to the Restricted Stock Award agreement shall be paid either: (A) in cash at the time of purchase; (B) at the discretion of the Board, according to a deferred payment or other similar arrangement with the Participant; or (C) in any other form of legal consideration that may be acceptable to the Board in its discretion; provided, however, that at any time that the Company is incorporated in Delaware, then payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

(iii) VESTING. Shares of Common Stock acquired under the Restricted Stock Award agreement may, but need not, be subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

(iv) TERMINATION OF PARTICIPANT'S CONTINUOUS SERVICE. In the event a Participant's Continuous Service terminates, the Company may repurchase or otherwise reacquire any or all of the shares of Common Stock held by the Participant which have not vested as of the date of termination under the terms of the Restricted Stock Award agreement.

(v) TRANSFERABILITY. Rights to acquire shares of Common Stock under the Restricted Stock Award agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the Restricted Stock Award agreement, as the Board shall determine in its discretion, so long as Common Stock awarded under the Restricted Stock Award agreement remains subject to the terms of the Restricted Stock Award agreement.

B -6

(c)PHANTOM STOCK AWARDS. Each Phantom Stock Award agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of Phantom Stock Award agreements may change from time to time, and the terms and conditions of separate Phantom Stock Award agreements need not be identical, provided, however, that each Phantom Stock Award agreement shall include (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i)CONSIDERATION. At the time of grant of a Phantom Stock Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Common Stock subject to the Phantom Stock Award. The consideration to be paid (if any) by the Participant for each share of Common Stock subject to a Phantom Stock Award may be paid in any form of legal consideration that may be acceptable to the Board in its sole discretion and permissible under applicable law.

(ii)VESTING. At the time of the grant of a Phantom Stock Award, the Board may impose such restrictions or conditions to the vesting of the Phantom Stock Award as it, in its sole discretion, deems appropriate.

(iii)PAYMENT. A Phantom Stock Award may be settled by the delivery of shares of Common Stock, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Phantom Stock Award agreement.

(iv)DIVIDEND EQUIVALENTS. Dividend equivalents may be credited in respect of shares of Common Stock covered by a Phantom Stock Award, as determined by the Board and contained in the Phantom Stock Award agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional shares of Common Stock covered by the Phantom Stock Award in such manner as determined by the Board. Any additional shares covered by the Phantom Stock Award credited by reason of such dividend equivalents will be subject to all the terms and conditions of the underlying Phantom Stock Award agreement to which they relate.

(v)TERMINATION OF PARTICIPANT'S CONTINUOUS SERVICE. Except as otherwise provided in the applicable Phantom Stock Award agreement, such portion of the Phantom Stock Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(vi)TRANSFERABILITY. Rights under the Phantom Stock Award agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the Phantom Stock Award agreement, as the Board shall determine in its discretion.

(d)STOCK APPRECIATION RIGHTS. Each Stock Appreciation Right agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of the Stock Appreciation Right agreements may change from time to time, and the terms and conditions of separate Stock Appreciation Right agreements need not be identical, but each Stock Appreciation Right agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i)CALCULATION OF APPRECIATION. Each Stock Appreciation Right will be denominated in shares of Common Stock equivalents. The appreciation distribution payable on the exercise of a Stock Appreciation Right will be not greater than an amount equal to the excess of (i) the aggregate Fair Market Value (on the date of the exercise of the Stock Appreciation Right) of a number of shares of Common Stock equal to the number of shares of Common Stock equivalents in which the Participant is vested under such Stock Appreciation Right, and with respect to which the Participant is exercising the Stock Appreciation Right on such date, over (ii) an amount (the strike price) that will be determined by the Board at the time of grant of the Stock Appreciation Right for such number of shares of Common Stock, provided that the strike price of a Stock Appreciation Right shall be not less than one hundred percent (100%) of the Fair Market Value of the Common Stock equal to the number of shares of Common Stock equivalents subject to the Stock Appreciation Right on the date the Stock Appreciation Right is granted.

(ii)VESTING. At the time of the grant of a Stock Appreciation Right, the Board may impose such restrictions or conditions to the vesting of such Stock Appreciation Right as it, in its sole discretion, deems appropriate.

(iii)EXERCISE. To exercise any outstanding Stock Appreciation Right, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Stock Appreciation Right agreement evidencing such Stock Appreciation Right.

(iv)PAYMENT. The appreciation distribution in respect to a Stock Appreciation Right may be paid in cash, shares of Common Stock, a combination of cash and shares of Common Stock or in any other form of consideration, as determined by the Board and contained in the Stock Appreciation Right agreement evidencing such Stock Appreciation Right.

B -7

(v)TERMINATION OF PARTICIPANT'S CONTINUOUS SERVICE. In the event that a Participant's Continuous Service terminates, the Participant may exercise his or her Stock Appreciation Right (to the extent that the Participant was entitled to exercise such Stock Appreciation Right as of the date of termination) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Participant's Continuous Service (or such longer or shorter period specified in the Stock Appreciation Right agreement), or (ii) the expiration of the term of the Stock Appreciation Right as set forth in the Stock Appreciation Right agreement. If, after termination, the Participant does not exercise his or her Stock Appreciation Right within the time specified herein or in the Stock Appreciation Right agreement (as applicable), the Stock Appreciation Right shall terminate.

(vi)TRANSFERABILITY. Rights under the Stock Appreciation Right agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the Stock Appreciation Right agreement, as the Board shall determine in its discretion.

8. COVENANTS OF THE COMPANY.

(a)AVAILABILITY OF SHARES. During the terms of the Stock Awards, the Company shall keep available at all times the number of shares of Common Stock required to satisfy such Stock Awards.

(b)SECURITIES LAW COMPLIANCE. The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise of the Stock Awards; provided, however, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any Common Stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell Common Stock upon exercise of such Stock Awards unless and until such authority is obtained.

9. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of Common Stock pursuant to Stock Awards shall constitute general funds of the Company.

10. MISCELLANEOUS.

(a)ACCELERATION OF EXERCISABILITY AND VESTING. The Board shall have the power to accelerate the time at which a Stock Award may first be exercised or the time during which a Stock Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Stock Award stating the time at which it may first be exercised or the time during which it will vest.

(b)STOCKHOLDER RIGHTS. No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to such Stock Award unless and until such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms.

(c)NO EMPLOYMENT OR OTHER SERVICE RIGHTS. Nothing in the Plan or any instrument executed or Stock Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or shall affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate or (iii) the service of a Director pursuant to the Bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(d)INCENTIVE STOCK OPTION \$100,000 LIMITATION. To the extent that the aggregate Fair Market Value (determined at the time of grant) of Common Stock with respect to which Incentive Stock Options are exercisable for the first time by any Optionholder during any calendar year (under all plans of the Company and its Affiliates) exceeds one hundred thousand dollars (\$100,000), the Options or portions thereof which exceed such limit (according to the order in which they were granted) shall be treated as Nonstatutory Stock Options.

(e)INVESTMENT ASSURANCES. The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant

is acquiring Common Stock subject to the Stock Award for the

B -8

Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (1) the issuance of the shares of Common Stock upon the exercise or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act or (2) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(f)WITHHOLDING OBLIGATIONS. To the extent provided by the terms of a Stock Award Agreement, the Participant may satisfy any federal, state or local tax withholding obligation relating to the exercise or acquisition of Common Stock under a Stock Award by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Participant by the Company) or by a combination of such means: (i) tendering a cash payment; (ii) authorizing the Company to withhold shares of Common Stock from the shares of Common Stock otherwise issuable to the Participant as a result of the exercise or acquisition of Common Stock under the Stock Award, provided, however, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law; or (iii) delivering to the Company owned and unencumbered shares of Common Stock.

11. ADJUSTMENTS UPON CHANGES IN STOCK.

(a)CAPITALIZATION ADJUSTMENTS. If any change is made in the Common Stock subject to the Plan, or subject to any Stock Award, without the receipt of consideration by the Company (through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company), the Plan will be appropriately adjusted in the class(es) and the number of securities subject to the Plan pursuant to subsection 4(a), the maximum number of securities subject to Stock Awards other than Options and Stock Appreciation Rights pursuant to subsection 4(d), the maximum number of securities subject to award to any person pursuant to subsection 5(c), and the outstanding Stock Awards will be appropriately adjusted in the class(es) and number of securities and price per share of Common Stock subject to such outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive. For clarity, the conversion of any convertible securities of the Company shall not be treated as a transaction "without receipt of consideration" by the Company.

(b)DISSOLUTION OR LIQUIDATION. In the event of a dissolution or liquidation of the Company, then all outstanding Stock Awards shall terminate immediately prior to such event.

(c)ASSET SALE, MERGER, CONSOLIDATION OR REVERSE MERGER. In the event of (i) a sale, lease or other disposition of all or substantially all of the assets of the Company, (ii) a merger or consolidation in which the Company is not the surviving corporation or (iii) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise, then any surviving corporation or acquiring corporation shall assume any Stock Awards outstanding under the Plan or shall substitute similar stock awards (including an award to acquire the same consideration paid to the stockholders in the transaction described in this subsection 11(c) for those outstanding under the Plan). In the event any surviving corporation or acquiring corporation fails to assume such Stock Awards or to substitute similar stock awards for those outstanding under the Plan, then with respect to Stock Awards held by Participants whose Continuous Service has not terminated, the vesting of such Stock Awards (and, if applicable, the time during which such Stock Awards may be exercised) shall be accelerated in full, and the Stock Awards shall terminate if not exercised (if applicable) at or prior to such event. With respect to any other Stock Awards outstanding under the Plan, such Stock Awards shall terminate if not exercised (if applicable) prior to such event.

12. AMENDMENT OF THE PLAN AND STOCK AWARDS.

(a)AMENDMENT OF PLAN. The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 11 relating to adjustments upon changes in Common Stock, no amendment shall be effective

unless approved by the stockholders of the Company to the extent stockholder approval is necessary to satisfy the requirements of Section 422 of the Code, Rule 16b-3 or any Nasdaq or securities exchange listing requirements.

(b)STOCKHOLDER APPROVAL. The Board may, in its sole discretion, submit any other amendment to the Plan for stockholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Section 162(m) of the Code and the regulations thereunder regarding the exclusion of performance-based compensation from the limit on corporate deductibility of compensation paid to certain executive officers.

(c)CONTEMPLATED AMENDMENTS. It is expressly contemplated that the Board may amend the Plan in any respect the Board deems necessary or advisable to provide eligible Employees with the maximum benefits provided or to be

B -9

provided under the provisions of the Code and the regulations promulgated thereunder relating to Incentive Stock Options and/or to bring the Plan and/or Incentive Stock Options granted under it into compliance therewith.

(d)NO IMPAIRMENT OF RIGHTS. Rights under any Stock Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

(e)AMENDMENT OF STOCK AWARDS. The Board at any time, and from time to time, may amend the terms of any one or more Stock Awards; provided, however, that the rights under any Stock Award shall not be impaired by any such amendment unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

13. TERMINATION OR SUSPENSION OF THE PLAN.

(a)PLAN TERM. The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate on the day before the tenth (10th) anniversary of the date the Plan is adopted by the Board or approved by the stockholders of the Company, whichever is earlier. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b)NO IMPAIRMENT OF RIGHTS. Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the Participant.

14. EFFECTIVE DATE OF PLAN.

The Plan shall become effective upon its adoption by the Board, but no Stock Award shall be exercised (or, in the case of a stock bonus, shall be granted) unless and until the Plan has been approved by the stockholders of the Company, which approval shall be within twelve (12) months before or after the date the Plan is adopted by the Board.

15. CHOICE OF LAW.

The law of the State of Delaware shall govern all questions concerning the construction, validity and interpretation of this Plan, without regard to such state's conflict of laws rules.

Appendix C

LEXICON PHARMACEUTICALS, INC.
NON-EMPLOYEE DIRECTORS' EQUITY INCENTIVE PLAN

This Plan initially was established as the 2000 Non-Employee Directors' Stock Option Plan, effective as of April 12, 2000 (the "2000 Non-Employee Directors' Stock Option Plan") which was adopted by the Board on February 3, 2000 and approved by the Company's stockholders on March 15, 2000. A subsequent amendment to the 2000 Non-Employee Directors' Stock Option Plan was approved by the Board on February 2, 2005 and approved by the Company's stockholders on April 27, 2005. The 2000 Non-Employee Directors' Stock Option Plan was subsequently amended and restated in its entirety and renamed the Non-Employee Directors' Stock Option Plan (the "Non-Employee Directors' Stock Option Plan"), which was adopted by the Board on February 27, 2009 and approved by the Company's stockholders on April 23, 2009. The Non-Employee Directors' Stock Option Plan is hereby amended and restated in its entirety and renamed the Non-Employee Directors' Equity Incentive Plan, effective as of its adoption by the Board subject to approval by the Company's stockholders. The terms of this Plan shall supersede the terms of 2000 Non-Employee Directors' Stock Option Plan and Non-Employee Directors' Stock Option Plan in their entirety.

1. PURPOSES.

- (a) **ELIGIBLE STOCK AWARD RECIPIENTS.** The persons eligible to receive Stock Awards are the Non-Employee Directors of the Company.
- (b) **AVAILABLE STOCK AWARDS.** The purpose of the Plan is to provide a means by which Non-Employee Directors may be given an opportunity to benefit from increases in value of the Common Stock through the granting of the following Stock Awards: (i) Nonstatutory Stock Options and (ii) Restricted Stock Awards.
- (c) **GENERAL PURPOSE.** The Company, by means of the Plan, seeks to retain the services of its Non-Employee Directors, to secure and retain the services of new Non-Employee Directors and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Affiliates.

2. DEFINITIONS.

- (a) **"AFFILIATE"** means any parent corporation or subsidiary corporation of the Company, whether now or hereafter existing, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.
- (b) **"ANNUAL GRANT"** means an Option and Restricted Stock Award granted annually to all Non-Employee Directors who meet the specified criteria pursuant to subsection 6(b) of the Plan.
- (c) **"ANNUAL MEETING"** means the annual meeting of the stockholders of the Company.
- (d) **"BOARD"** means the Board of Directors of the Company.
- (e) **"CODE"** means the Internal Revenue Code of 1986, as amended.
- (f) **"COMMON STOCK"** means the common stock, par value \$.001 per share, of the Company.
- (g) **"COMPANY"** means Lexicon Pharmaceuticals, Inc., a Delaware corporation.
- (h) **"CONSULTANT"** means any person other than a Director or Employee who is engaged by the Company or an Affiliate to render consulting or advisory services and who is compensated for such services.
- (i) **"CONTINUOUS SERVICE"** means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. The Participant's Continuous Service shall not be deemed to have terminated merely because of a change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's Continuous Service. For example, a change in status from a Non-Employee Director of the Company to a Consultant of an Affiliate or an Employee of the Company will not constitute an interruption of Continuous Service. The Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave.
- (j) **"DIRECTOR"** means a member of the Board of Directors of the Company.

C -1

- (k) “DISABILITY” means the permanent and total disability of a person within the meaning of Section 22(e)(3) of the Code.
- (l) “EMPLOYEE” means any person employed by the Company or an Affiliate. Mere service as a Director or payment of a director's fee by the Company or an Affiliate shall not be sufficient to constitute “employment” by the Company or an Affiliate.
- (m) “EXCHANGE ACT” means the Securities Exchange Act of 1934, as amended.
- (n) “FAIR MARKET VALUE” means, as of any date, the value of the Common Stock determined as follows:
- (i) If the Common Stock is listed on any established stock exchange or traded on the Nasdaq Stock Market, the Fair Market Value of a share of Common Stock shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the last market trading day prior to the day of determination, as reported in The Wall Street Journal or such other source as the Board deems reliable.
- (ii) In the absence of such markets for the Common Stock, the Fair Market Value shall be determined in good faith by the Board in such manner as it deems appropriate and as is consistent with the requirements of section 409A of the Code.
- (o) “INITIAL GRANT” means an Option granted to a Non-Employee Director who meets the specified criteria pursuant to subsection 6(a) of the Plan.
- (p) “NON-EMPLOYEE DIRECTOR” means a Director who is not an Employee.
- (q) “NONSTATUTORY STOCK OPTION” means an option to purchase Common Stock that is not intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.
- (r) “OPTION” means a Nonstatutory Stock Option to purchase Common Stock granted pursuant to the Plan.
- (s) “PARTICIPANT” means any Non-Employee Director to whom a Stock Award is granted pursuant to the Plan.
- (t) “PLAN” means this Lexicon Pharmaceuticals, Inc. Non-Employee Directors' Equity Incentive Plan.
- (u) “RESTRICTED STOCK AWARD” means a right to receive restricted Common Stock granted pursuant to the Plan.
- (v) “RULE 16B-3” means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.
- (w) “SECURITIES ACT” means the Securities Act of 1933, as amended.
- (x) “STOCK AWARD” means any Option or Restricted Stock Award granted under the Plan.
- (y) “STOCK AWARD AGREEMENT” means a written agreement between the Company and a holder of a Stock Award evidencing the terms and conditions of an individual Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.

3. ADMINISTRATION.

- (a) ADMINISTRATION BY BOARD. The Board shall administer the Plan. The Board may not delegate administration of the Plan to a committee.
- (b) POWERS OF BOARD. The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:
- (i) To determine the provisions of each Stock Award to the extent not specified in the Plan.
- (ii) To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

- (iii) To amend the Plan or a Stock Award as provided in Section 13.
- (iv) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company that are not in conflict with the provisions of the Plan.
- (c) EFFECT OF BOARD'S DECISION. All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

4. SHARES SUBJECT TO THE PLAN.

- (a) SHARE RESERVE. Subject to the provisions of Section 12 relating to adjustments upon changes in the Common Stock, the Common Stock that may be issued pursuant to Stock Awards shall not exceed in the aggregate one million, five hundred thousand (1,500,000) shares of Common Stock.
- (b) REVERSION OF SHARES TO THE SHARE RESERVE. If any Stock Award shall for any reason expire or otherwise terminate, in whole or in part, without the shares of Common Stock issuable thereunder being issued in full, the shares of Common Stock not issued under such Stock Award shall revert to and again become available for issuance under the Plan. For clarity, shares subject to an Option that are not delivered to a Participant because (i) such Participant's right to purchase such shares are surrendered in payment of the exercise price for other shares subject to such Option in a "net exercise," or (ii) such shares are withheld in satisfaction of the withholding of taxes incurred in connection with the exercise of such Option, the shares so surrendered or withheld shall not remain available for subsequent issuance under the Plan.
- (c) SOURCE OF SHARES. The shares of Common Stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

5. ELIGIBILITY.

The Stock Awards as set forth in section 6 automatically shall be granted under the Plan to all Non-Employee Directors.

6. NON-DISCRETIONARY GRANTS.

- (a) INITIAL GRANTS. Without any further action of the Board, each person who is elected or appointed for the first time to be a Non-Employee Director automatically shall, upon the date of his or her initial election or appointment to be a Non-Employee Director, be granted an Option to purchase Thirty Thousand (30,000) shares of Common Stock on the terms and conditions set forth herein.
- (b) ANNUAL GRANTS. Without any further action of the Board, on the day following each Annual Meeting, each person who is then a Non-Employee Director, and has been a Non-Employee Director for at least six (6) months, automatically shall be granted (i) an Option to purchase Twenty Thousand (20,000) shares of Common Stock and (ii) a Restricted Stock Award to receive the number of shares of Common Stock determined by dividing \$20,000 by the Fair Market Value of the Common Stock on the date the Restricted Stock Award is granted, rounded down to the nearest whole share number, each such Option and Restricted Stock Award to be granted on the terms and conditions set forth herein.

7. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as required by the Plan. Each Option shall contain such additional terms and conditions, not inconsistent with the Plan, as the Board shall deem appropriate. Each Option shall include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

- (a) TERM. No Option shall be exercisable after the expiration of ten (10) years from the date it was granted.
- (b) EXERCISE PRICE. The exercise price of each Option shall be one hundred percent (100%) of the Fair Market Value of the stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.
- (c) CONSIDERATION. The purchase price of stock acquired pursuant to an Option may be paid, to the extent permitted by applicable statutes and regulations, in any combination of (i) cash or check, (ii) delivery to the Company of other Common Stock, or (iii) surrender of Participant's right to purchase shares subject to such Option (valued, for such purposes, as the Fair Market Value of such surrendered shares on the date of exercise less the exercise price for such surrendered shares) in payment of the exercise price for other shares subject to such Option in a "net exercise" of

such Option.

C -3

(d) **TRANSFERABILITY.** An Option is not transferable, except (i) by will or by the laws of descent and distribution, (ii) by instrument to an inter vivos or testamentary trust, in a form accepted by the Company, in which the Option is to be passed to beneficiaries upon the death of the trustor (settlor) and (iii) by gift, in a form accepted by the Company, to a member of the “immediate family” of the Participant as that term is defined in 17 C.F.R. 240.16a-1(e). In addition, the Participant may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Participant, shall thereafter be entitled to exercise the Option.

(e) **VESTING.** Options shall vest as follows:

(i) Initial Grants of Options shall provide for vesting of 1/60th of the shares subject to the Option each month after grant for five (5) years after the date of the grant.

(ii) Annual Grants of Options shall provide for vesting of 1/12th of the shares subject to the Option each month after grant for twelve (12) months after the date of the grant.

(f) **TERMINATION OF CONTINUOUS SERVICE.** In the event an Participant's Continuous Service terminates (other than upon the Participant's death or Disability), the Participant may exercise his or her Option (to the extent that the Participant was entitled to exercise it as of the date of termination) but only within such period of time ending on the earlier of (i) the date six (6) months following the termination of the Participant's Continuous Service, or (ii) the expiration of the term of the Option as set forth in the Stock Award Agreement. If, after termination, the Participant does not exercise his or her Option within the time specified in the Stock Award Agreement, the Option shall terminate.

(g) **EXTENSION OF TERMINATION DATE.** If the exercise of the Option following the termination of the Participant's Continuous Service (other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of shares would violate the registration requirements under the Securities Act, then the Option shall terminate on the earlier of (i) the expiration of the term of the Option set forth in subsection 7(a) or (ii) the expiration of a period of three (3) months after the termination of the Participant's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements.

(h) **DISABILITY OF PARTICIPANT.** In the event an Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Option (to the extent that the Participant was entitled to exercise it as of the date of termination), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination or (ii) the expiration of the term of the Option as set forth in the Stock Award Agreement. If, after termination, the Participant does not exercise his or her Option within the time specified herein, the Option shall terminate.

(i) **DEATH OF PARTICIPANT.** In the event (i) an Participant's Continuous Service terminates as a result of the Participant's death or (ii) the Participant dies within the three-month period after the termination of the Participant's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Participant was entitled to exercise the Option as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated to exercise the Option upon the Participant's death, but only within the period ending on the earlier of (A) the date eighteen (18) months following the date of death or (B) the expiration of the term of such Option as set forth in the Stock Award Agreement. If, after death, the Option is not exercised within the time specified herein, the Option shall terminate.

8. RESTRICTED STOCK AWARD PROVISIONS.

Each Restricted Stock Award shall be in such form and shall contain such terms and conditions as required by the Plan. Each Restricted Stock Award shall contain such additional terms and conditions, not inconsistent with the Plan, as the Board shall deem appropriate. Each Restricted Stock Award shall include (through incorporation of provisions hereof by reference in the Restricted Stock Award or otherwise) the substance of each of the following provisions:

(a) **CONSIDERATION.** The shares of Common Stock underlying Restricted Stock Awards shall be issued to the Participant for no further consideration.

(b) **TRANSFERABILITY.** A Restricted Stock Award is not transferable, except (i) by will or by the laws of descent and distribution, (ii) by instrument to an inter vivos or testamentary trust, in a form accepted by the Company, in which the Restricted Stock Award is to be passed to beneficiaries upon the death of the trustor (settlor) and (iii) by gift, in a form accepted by the Company, to a member of the “immediate family” of the Participant as that term is

defined in 17 C.F.R. 240.16a-1(e).

(c) VESTING. Unless otherwise determined by the Board, the shares of Common Stock underlying Restricted Stock Awards shall not be subject to any vesting or share repurchase option in favor of the Company.

C -4

9. COVENANTS OF THE COMPANY.

(a) AVAILABILITY OF SHARES. During the terms of the Stock Awards, the Company shall keep available at all times the number of shares of Common Stock required to satisfy such Stock Awards.

(b) SECURITIES LAW COMPLIANCE. The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise or grant of the Stock Awards; provided, however, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell Common Stock upon exercise or grant of such Stock Awards unless and until such authority is obtained.

10. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of Common Stock pursuant to Options shall constitute general funds of the Company.

11. MISCELLANEOUS.

(a) STOCKHOLDER RIGHTS. No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares subject to such Stock Award unless and until such Participant has satisfied all requirements for the acquisition of shares of Common Stock underlying the Stock Award pursuant to its terms.

(b) NO SERVICE RIGHTS. Nothing in the Plan or any instrument executed or Stock Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company as a Non-Employee Director or shall affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate or (iii) the service of a Director pursuant to the Bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(c) INVESTMENT ASSURANCES. The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring the Common Stock subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (iii) the issuance of the shares upon the exercise or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act or (iv) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(d) WITHHOLDING OBLIGATIONS. The Participant may satisfy any federal, state or local tax withholding obligation relating to the exercise or acquisition of Common Stock under a Stock Award by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Participant by the Company) or by a combination of such means: (i) tendering a cash payment; (ii) authorizing the Company to withhold shares from the shares of the Common Stock otherwise issuable to the Participant as a result of the exercise or acquisition of stock under the Stock Award, provided, however, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law; or (iii) delivering to the Company owned and unencumbered shares of the Common Stock.

12. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) CAPITALIZATION ADJUSTMENTS. If any change is made in the stock subject to the Plan, or subject to any Stock Award, without the receipt of consideration by the Company (through merger, consolidation, reorganization,

recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company), the Plan will be appropriately adjusted in the class(es) and number of securities subject to the Plan pursuant to subsection 4(a)

C -5

and to be granted as nondiscretionary Options and Restricted Stock Awards specified in Section 5, and the outstanding Stock Awards will be appropriately adjusted in the class(es) and number of securities and price per share of stock subject to such outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive. For clarity, the conversion of any convertible securities of the Company shall not be treated as a transaction “without receipt of consideration” by the Company.

(b) **DISSOLUTION OR LIQUIDATION.** In the event of a dissolution or liquidation of the Company, then all outstanding Stock Awards shall terminate immediately prior to such event.

(c) **ASSET SALE, MERGER, CONSOLIDATION OR REVERSE MERGER.**

(i) In the event of (i) a sale, lease or other disposition of all or substantially all of the assets of the Company, (ii) a merger or consolidation in which the Company is not the surviving corporation or (iii) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise, then any surviving corporation or acquiring corporation shall assume any Stock Awards outstanding under the Plan or shall substitute similar stock awards (including an award to acquire the same consideration paid to the stockholders in the transaction described in this subsection 12(c) for those outstanding under the Plan).

(ii) In the event any surviving corporation or acquiring corporation refuses to assume such Stock Awards or to substitute similar stock awards for those outstanding under the Plan, then the vesting of such Stock Awards shall be accelerated in full, and the Stock Awards shall terminate if not exercised (if applicable) at or prior to such event.

(iii) In the event any surviving corporation or acquiring corporation assumes such Stock Awards or substitutes similar stock awards for those outstanding under the Plan but the Participant is not elected or appointed to the board of directors of the surviving corporation or acquiring corporation at the first meeting of such board of directors after such change in control event, then the vesting of such Stock Awards shall be accelerated by eighteen (18) months on the day after the first meeting of the board of directors of the surviving corporation or acquiring corporation.

(iv) In the event any surviving corporation or acquiring corporation assumes such Stock Awards or substitutes similar stock awards for those outstanding under the Plan and the Participant is elected or appointed to the board of directors of the surviving corporation or acquiring corporation at the first meeting of such board of directors after such change in control event, then the vesting of such Stock Awards shall not be accelerated.

13. AMENDMENT OF THE PLAN AND STOCK AWARDS.

(a) **AMENDMENT OF PLAN.** The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 12 relating to adjustments upon changes in stock, no amendment shall be effective unless approved by the stockholders of the Company to the extent stockholder approval is necessary to satisfy the requirements of Rule 16b-3 or any Nasdaq or other securities exchange listing requirements.

(b) **STOCKHOLDER APPROVAL.** The Board may, in its sole discretion, submit any other amendment to the Plan for stockholder approval.

(c) **NO IMPAIRMENT OF RIGHTS.** Rights under any Option granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

(d) **AMENDMENT OF STOCK AWARDS.** The Board at any time, and from time to time, may amend the terms of any one or more Stock Awards; provided, however, that the rights under any Stock Award shall not be impaired by any such amendment unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

14. TERMINATION OR SUSPENSION OF THE PLAN.

(a) **PLAN TERM.** The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate on the day before the tenth (10th) anniversary of the date the Plan is adopted by the Board or approved by the stockholders of the Company, whichever is earlier. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) **NO IMPAIRMENT OF RIGHTS.** Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the Participant.

15. EFFECTIVE DATE OF PLAN.

The Plan shall become effective as determined by the Board, but no Option shall be exercised and no Restricted Stock Award shall be granted unless and until the Plan has been approved by the stockholders of the Company, which approval shall be within twelve (12) months before or after the date the Plan is adopted by the Board.

16. CHOICE OF LAW.

All questions concerning the construction, validity and interpretation of this Plan shall be governed by the law of the State of Delaware, without regard to such state's conflict of laws rules.

C -7

LEXICON PHARMACEUTICALS, INC.
 8800 TECHNOLOGY FOREST PLACE
 THE WOODLANDS, TX 77381

VOTE BY INTERNET - www.proxyvote.com

Use the Internet to transmit your voting instructions and for electronic delivery of information up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. 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 up until 11:59 P.M. Eastern Time the day before the cut-off date or meeting date. 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

| | | |
|---------|--|---|
| | 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 | |
| For All | Withhold For All Except | |
| o | o | o |

The Board of Directors recommends you vote FOR the following

- | | | |
|-----------------------------------|------------------------|-----------------------|
| 1. Election of Directors | | |
| Nominees | | |
| 01 Arthur T. Sands M.D., Ph.D. | 02 Philippe J. Amouyal | 03 Frank P. Palantoni |

| | | | |
|--|-----|---------|---------|
| The Board of Directors recommend you vote FOR proposals 2 through 6: | For | Against | Abstain |
| 2. | o | o | o |

Ratification and approval of the Company's amended and restated certificate of incorporation

- | | | | | |
|----|--|---|---|---|
| 3. | Ratification and approval of the amendment to the Company's Equity Incentive Plan | o | o | o |
| 4. | Ratification and approval of the amendment to the Company's Non-Employee Directors' Stock Option Plan | o | o | o |
| 5. | Advisory vote on the compensation paid to the Company's named executive officers | o | o | o |
| 6. | Ratification and approval of the appointment of Ernst & Young LLP as the Company's independent auditors for the fiscal year ending December 31, 2012 | o | o | 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
April 26, 2012
This Proxy is solicited by the Board of Directors

The stockholder(s) hereby appoint(s) Arthur T. Sands, M.D., Ph.D. 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 April 26, 2012 at the offices of the company, 8800 Technology Forest Place, The Woodlands, Texas, 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