

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

**SCHEDULE 14A**

Proxy Statement Pursuant to Section 14(a) of the Securities  
Exchange Act of 1934 (Amendment No. 1)

Filed by the Registrant   
Filed by a Party other than the Registrant

Check the appropriate box:

- Preliminary Proxy Statement
- Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))**
- Definitive Proxy Statement
- Definitive Additional Materials
- Soliciting Material Pursuant to §240.14a-12

LEXICON PHARMACEUTICALS, INC.

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

- No fee required.
- Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.

(1) Title of each class of securities to which transaction applies:

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(2) Aggregate number of securities to which transaction applies:

\_\_\_\_\_

(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):

\_\_\_\_\_

(4) Proposed maximum aggregate value of transaction:

\_\_\_\_\_

(5) Total fee paid:

\_\_\_\_\_

Fee paid previously with preliminary materials.

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:

\_\_\_\_\_

\_\_\_\_\_



**YOUR VOTE IS VERY IMPORTANT**

To our stockholders:

Our board of directors has called a special meeting of stockholders, as described in the enclosed notice of special meeting of stockholders and proxy statement. The special meeting is being called so that our stockholders may consider and act upon matters necessary to enable us to raise capital through the issuance of additional shares of our common stock. At the special meeting our stockholders will be asked to approve (1) a transaction with Invus, L.P., an affiliate of The Invus Group, LLC, which will include the issuance of approximately 50.8 million shares of our common stock to Invus for approximately \$205 million and may include the issuance of additional shares of our common stock in up to two rights offerings, and (2) an amendment to our certificate of incorporation necessary for us to issue the shares.

The Invus transaction will provide us with needed additional capital and the financial flexibility to, among other things, implement a long-term financial strategy to fund our extensive drug discovery and development pipeline. By enabling us to pursue this strategy, we believe the Invus transaction will allow us to better realize the potential of our discoveries as breakthrough pharmaceutical products, and to capture a greater proportion of the benefits of those products for our stockholders. Your approval of the Invus transaction will allow us to establish a firm financial foundation upon which we can build an integrated biopharmaceutical company.

The Invus transaction will require the affirmative vote of a majority of all of the outstanding shares of our common stock with respect to the amendment to our certificate of incorporation. If the holders of less than a majority of the outstanding shares of our common stock vote in favor of the amendment to our certificate of incorporation, we will not be able to complete the Invus financing and may not be able to implement our strategy. We therefore urge you to participate.

The special meeting will be held:

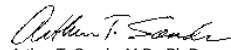
Thursday, August 23, 2007  
1:30 p.m., local time  
The Marriott Woodlands Waterway Hotel and Convention Center  
1601 Lake Robbins Drive  
The Woodlands, Texas

This proxy statement provides detailed information about the Invus transaction and the special meeting. We encourage you to read the entire proxy statement carefully.

**Our board of directors has unanimously approved the Invus transaction and the amendment to our certificate of incorporation, has determined that the Invus transaction and the amendment to our certificate of incorporation are advisable and in the best interest of our stockholders and unanimously recommends that you vote for the Invus transaction and for the amendment to our certificate of incorporation.**

Your vote is important, regardless of the number of shares you own. Please vote as soon as possible to make sure that your shares are represented at the special meeting. To vote your shares, please complete and return the enclosed proxy card, or use telephone or Internet voting. You also may cast your vote in person at the special meeting.

Sincerely,

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

This proxy statement is dated July 20, 2007, and is first being mailed to stockholders on or about July 24, 2007.

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**LEXICON PHARMACEUTICALS, INC.**

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

**NOTICE OF SPECIAL MEETING OF STOCKHOLDERS  
TO BE HELD AUGUST 23, 2007**

TO OUR STOCKHOLDERS:

A special meeting of the stockholders of Lexicon Pharmaceuticals, Inc. will be held on August 23, 2007 at 1:30 p.m., local time, at The Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas, to:

1. approve the Invus transaction, which includes, among other things, the issuance by us of approximately 50.8 million shares of our common stock for approximately \$205 million and may include the issuance of additional shares of our common stock in up to two rights offerings pursuant to a securities purchase agreement between us and Invus, L.P., dated as of June 17, 2007, as it may be amended from time to time;
2. amend our certificate of incorporation to increase the number of authorized shares of our common stock from 120 million to 300 million; and
3. act on any other business that properly comes before the special meeting or any adjournment or postponement of the special meeting.

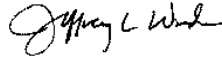
You are entitled to vote at the special meeting or any adjournment or postponement of the special meeting only if you were the record owner of shares of our common stock at the close of business on July 19, 2007.

The Marketplace Rules of the Nasdaq Stock Market, on which our common stock is quoted, require stockholder approval of the issuance of securities contemplated by the Invus transaction.

The effectuation of the proposal on the Invus transaction is conditioned on the approval of the proposed amendment to our certificate of incorporation. The Invus transaction will not be completed, even if all other conditions under the securities purchase agreement are satisfied or waived, if the requisite stockholder approval on both proposals is not received. Accordingly, if you wish to approve the Invus transaction, you must vote to approve both the amendment to our certificate of incorporation and the Invus transaction. However, the effectuation of the proposal on the amendment to our certificate of incorporation is not conditioned on the approval of the proposal on the Invus transaction. If the proposal on the amendment to our certificate of incorporation is approved, we plan to effect the amendment.

It is important that your shares be represented at the special meeting whether or not you plan to attend. **Please mark, sign and date the enclosed proxy and return it in the accompanying postpaid envelope as promptly as possible, or use telephone or internet voting.** If you are present at the special meeting, and wish to do so, you may revoke your proxy and vote in person.

By order of the board of directors,



Jeffrey L. Wade  
Secretary

The Woodlands, Texas  
July 20, 2007

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## SUMMARY

*This summary highlights selected information from this proxy statement and may not contain all of the information that is important to you. To understand fully the proposals to be acted upon, you should carefully read the entire proxy statement, including the attached annexes.*

**Lexicon Pharmaceuticals, Inc.** Lexicon Pharmaceuticals, Inc. is a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We currently have clinical programs underway for such areas of major unmet medical need as irritable bowel syndrome and cognitive disorders. We have used our proprietary gene knockout technology to discover more than 100 promising drug targets and create an extensive pipeline of clinical and preclinical programs in the therapeutic areas of diabetes and obesity, cardiovascular disease, psychiatric and neurological disorders, cancer, immune system disorders and ophthalmic disease. To advance the development and commercialization of our programs, we are working both independently and through collaborators including Bristol-Myers Squibb Company, Genentech, Inc., N.V. Organon and Takeda Pharmaceutical Company Limited.

**The Invus Group, LLC.** The Invus Group, LLC is a New York-based investment firm with additional offices in London and Paris. Invus invests in a variety of equity transactions, including buyouts, longer term public equity investments, venture capital, and expansion financings. The Invus Group and its affiliates manage in excess of \$4 billion of capital in a broad range of industries, including consumer goods, consumer services, biotechnology, medical devices, education and software. In this proxy statement, we use Invus to refer to Invus, L.P., an affiliate of The Invus Group, LLC, which is a party to the agreements governing the transaction described in this proxy statement.

**The Invus Transaction.** On June 17, 2007, we and Invus entered into a securities purchase agreement, a warrant agreement, a stockholders' agreement and a registration rights agreement, each of which has been unanimously approved by our board of directors. Pursuant to the warrant agreement, Invus has received warrants to purchase up to 16,498,353 shares of our common stock, for a per share purchase price of \$3.0915, the average of the volume-weighted average prices per share of our common stock over the ten trading days ended June 14, 2007. The issuance and purchase of shares upon the exercise of the warrants are not subject to stockholder approval. Pursuant to the securities purchase agreement, upon stockholder approval, Invus will purchase, at that price, a number of shares approximately equal to the number of shares that remain subject to the warrants, and the warrants will terminate. Invus also will purchase approximately 34.3 million additional shares of our common stock for a per share purchase price of \$4.50, representing a 46% premium to the per share closing price of our common stock on June 15, 2007, the last trading day before the securities purchase agreement was signed. Combined, these purchases for approximately \$205 million (which we refer to as the initial investment) will bring Invus' ownership to 40% of the post-transaction outstanding shares of our common stock. Invus will have the right to designate three members of our board of directors at the closing of the initial investment.

To assure long-term adequate financing, Invus will also have the right to require us to initiate up to two pro rata rights offerings to our stockholders, which would provide all stockholders with non-transferable rights to acquire shares of our common stock, in an aggregate amount of up to approximately \$345 million, less the proceeds of any "qualified offerings" that we may complete in the interim involving the sale of our common stock at prices above \$4.50 per share. The first rights offering may be initiated, subject to certain adjustments, beginning on the date that is 27 months from the closing of the initial investment, and the second rights offering may be initiated beginning on the date that is later of 12 months after the initiation of the first rights offering and 39 months from the closing of the initial investment if the first rights offering does not take place. The initial investment and subsequent rights offerings, combined with any qualified offerings, are designed to achieve up to \$550 million in proceeds to us. Invus would participate in each rights offering for up to its pro rata portion of the offering, and would commit to purchase the entire portion of the offering not subscribed for by other stockholders.

The material terms of each of the securities purchase agreement, the warrant agreement, the stockholders' agreement and the registration rights agreement are described in more detail in this proxy statement under the heading "Proposal One — The Invus Transaction." These agreements have been filed with the SEC as exhibits

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to our Current Report on Form 8-K filed on June 19, 2007. We refer to the transactions contemplated by these agreements as the Invus transaction in this proxy statement. Stockholders are being asked to vote on the entire Invus transaction and, if the Invus transaction and the amendment to our certificate of incorporation are approved, no further stockholder approval will be sought for any element of the transaction.

*Reasons for the Invus Transaction.* The Invus transaction will provide us with needed additional capital and the financial flexibility to, among other things, implement a long-term financial strategy that will:

- fund our extensive drug discovery and development pipeline;
- enhance our internal clinical and regulatory capabilities; and
- allow us to pursue a collaboration and licensing strategy that is less subject to short-term financing pressures.

In addition to the \$205 million initial investment, the Invus transaction establishes a financial framework for future funding that may provide up to an additional \$345 million from a combination of qualified offerings at prices per share above \$4.50 and rights offerings in which all of our stockholders may participate. We believe that the structure of the Invus transaction provides a framework for obtaining future funding by means that are favorable to all of our stockholders.

By enabling us to pursue a long-term financial strategy, we believe the Invus transaction will allow us to better realize the potential of our discoveries as breakthrough pharmaceutical products, and to capture a greater proportion of the benefits of those products for our stockholders. Your approval of the Invus transaction will allow us to establish a firm financial foundation upon which we can build an integrated biopharmaceutical company.

*Opinion of Financial Advisor.* In connection with the Invus transaction, our board of directors received the opinion of Morgan Stanley & Co. Incorporated, financial advisor to our board of directors, to the effect that, as of the date of such opinion, the consideration to be received by us in connection with the initial investment pursuant to the securities purchase agreement was fair from a financial point of view to us. The full text of the written opinion of Morgan Stanley, dated June 16, 2007, is included as Annex B to this proxy statement and is incorporated herein by reference. You should read the opinion carefully in its entirety for a description of the assumptions made, the matters considered and limitations on the review undertaken. Morgan Stanley addressed its opinion to our board of directors, and the opinion does not constitute a recommendation to any stockholder as to how to vote or as to any other action that a stockholder should take relating to the Invus transaction.

*Conditions to the Completion of the Invus Transaction.* The completion of the Invus transaction is subject to the satisfaction or waiver of a number of conditions, including the approval by our stockholders of the Invus transaction and the amendment to our certificate of incorporation. These and other conditions are summarized in this proxy statement under the heading "Proposal One — The Invus Transaction — Securities Purchase Agreement — Conditions."

*Termination.* The securities purchase agreement may be terminated in certain instances, including if stockholder approval of the Invus transaction and the amendment to our certificate of incorporation is not obtained. See "Proposal One — The Invus Transaction — Securities Purchase Agreement — Termination." If the securities purchase agreement is terminated, the warrants will remain exercisable for a period of time extending beyond the date of such termination unless the termination is due to a material breach by Invus. See "Proposal One — The Invus Transaction — Warrant Agreement — Exercise Period of Warrants."

*Amendment to our Certificate of Incorporation.* Our stockholders are also being asked to approve an amendment to our certificate of incorporation that would increase the number of authorized shares of our common stock from 120 million to 300 million (see "Proposal Two — Amendment to our Certificate of Incorporation to Increase our Authorized Shares of Common Stock").

The approval of this amendment to our certificate of incorporation is a condition to the consummation of the Invus transaction. The amendment to our certificate of incorporation will be contained in a certificate of

amendment of our certificate of incorporation, a form of which is attached as Annex A to this proxy statement.

*Stockholder Votes Required.* In accordance with the Marketplace Rules of The Nasdaq Stock Market, approval of the Invus transaction requires the approval of the holders of a majority of the total votes cast by holders of shares of our common stock on such proposal, provided that a majority of the outstanding shares of our common stock are represented at the meeting. The approval of the amendment to our certificate of incorporation requires the approval of the holders of a majority of the outstanding shares of our common stock.

The Invus transaction is conditioned upon the amendment to our certificate of incorporation. If our stockholders approve the Invus transaction but do not approve the amendment to our certificate of incorporation, the Invus transaction will not be consummated.

The amendment to our certificate of incorporation is not conditioned on the Invus transaction. If our stockholders approve the amendment to our certificate of incorporation but do not approve the Invus transaction, we plan to effect the amendment.

*Recommendation to Stockholders.* Our board of directors has unanimously approved the Invus transaction and the amendment to our certificate of incorporation, has determined that the Invus transaction and the amendment to our certificate of incorporation are advisable and in the best interest of our stockholders and unanimously recommends that you vote FOR the Invus transaction and that you vote FOR the amendment to our certificate of incorporation.

*Warrants.* Concurrently with the execution of securities purchase agreement, we entered into a warrant agreement with Invus under which we have issued to Invus warrants to purchase up to 16,498,353 shares of our common stock at an exercise price of \$3.0915 per share. As indicated above, purchases of shares upon exercise of the warrants prior to the closing of the initial investment are not subject to stockholder approval and will reduce the number of shares to be purchased by Invus at the same price in the initial investment. If the initial investment is completed, any warrants not exercised prior to the closing of the initial investment will automatically terminate.

*Registration Rights Agreement.* Concurrently with the execution of the securities purchase agreement, we entered into a registration rights agreement with Invus under which we granted Invus certain registration rights with respect to shares of our common stock purchased under the securities purchase agreement and upon the exercise of the warrants.

*Stockholders' Agreement.* Concurrently with the execution of the securities purchase agreement, we entered into a stockholders' agreement with Invus under which Invus will have the right to designate three members of our board of directors at the closing of the initial investment. From and after the first anniversary of the closing of the initial investment, Invus' right to designate members of our board of directors will be determined based on Invus' percentage ownership of our common stock, as described below under the heading "Proposal One — The Invus Transaction — Stockholders' Agreement." These same directors designated by Invus could, at Invus' request, have proportionate representation on the board of directors of any subsidiary or on each committee of our and our subsidiaries' boards of directors.

Under the stockholders' agreement, Invus will also be subject to certain standstill restrictions, as well as restrictions on the transfer and voting of the shares of common stock held by it and its affiliates, and, as long as Invus holds at least 15% of the total number of outstanding shares of our common stock, Invus will be entitled to certain minority protections. These provisions are detailed below under the heading "Proposal One — The Invus Transaction — Stockholders' Agreement."

*Where You Can Find More Information.* 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.

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission, or the SEC. You may read and copy any reports, statements or other information

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we file at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C., 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from the web site maintained by the SEC at [www.sec.gov](http://www.sec.gov).

We filed a Current Report on Form 8-K on June 19, 2007 reporting the execution of the securities purchase agreement by us and Invus. A copy of the securities purchase agreement and related documents are filed as exhibits to the Form 8-K.

**THE SPECIAL MEETING**

Our board of directors is sending this proxy statement and the enclosed proxy card to solicit proxies from our stockholders for use at a special meeting and at any postponement or adjournment thereof to vote for approval of the Invus transaction and the amendment to our certificate of incorporation. We are first mailing the notice of special meeting of stockholders, this proxy statement and the enclosed proxy card to our stockholders on or about July 24, 2007.

**Date, Time and Place of Special Meeting**

August 23, 2007  
1:30 p.m., local time  
The Marriott Woodlands Waterway Hotel and Convention Center  
1601 Lake Robbins Drive  
The Woodlands, Texas

**Purpose of Meeting**

The purpose of the meeting is to vote on the following items:

1. A proposal to approve the Invus transaction, which includes, among other things, the issuance by us of approximately 50.8 million shares of our common stock for approximately \$205 million and may include the issuance of additional shares of our common stock in up to two rights offerings pursuant to a securities purchase agreement between us and Invus, dated as of June 17, 2007, as it may be amended from time to time.
2. A proposal to amend our certificate of incorporation to increase the number of authorized shares of our common stock from 120 million to 300 million.

**Shares Entitled To Vote**

You are entitled to vote at the special 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 July 19, 2007, the record date for the special meeting established by our board of directors.

**How to Vote Your Shares**

You may vote in person at the special meeting or by proxy. To ensure that your shares are represented at the special meeting, we recommend you vote by proxy even if you plan to attend the special meeting in person. Even if you vote by proxy, if you wish, you can revoke your proxy and vote in person at the special meeting. If you want to vote at the special 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 July 19, 2007 or a proxy to vote your shares.

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



**Quorum**

We must have a quorum to conduct any business at the special meeting. This means that at least a majority of our outstanding shares eligible to vote at the special meeting must be represented at the special meeting, either in person or by proxy. Abstentions are counted for purposes of determining whether a quorum is present. In addition, shares of our common stock held by intermediaries that are voted for at least one matter at the special meeting will be counted as being present for purposes of determining a quorum for all matters, 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").

**Outstanding Shares**

On the record date, we had 85,965,249 shares of our common stock 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 special meeting or at any postponement or adjournment thereof.

**Vote Necessary to Approve the Proposals**

1. To approve the Invus transaction, it is necessary to obtain the affirmative vote of the holders of shares (in person or by proxy) of our common stock as of the record date representing a majority of the total votes cast at the meeting.

2. To approve the amendment to our certificate of incorporation, it is necessary to obtain the affirmative vote of the holders of shares (in person or by proxy) of our common stock as of the record date representing a majority of the outstanding shares of our common stock.

The effectuation of the proposal on the Invus transaction is conditioned on the approval of the proposed amendment to our certificate of incorporation. The Invus transaction will not be completed, even if all other conditions under the securities purchase agreement are satisfied or waived, if the requisite stockholder approval on both proposals is not received. Accordingly, if you wish to approve the Invus transaction, you must vote to approve the amendment to our certificate of incorporation and the Invus transaction. However, the effectuation of the proposal on the amendment to our certificate of incorporation is not conditioned on the approval of the proposal on the Invus transaction. If the proposal on the amendment to our certificate of incorporation is approved, we plan to effect the amendment.

Our board of directors unanimously recommends that our stockholders vote FOR the Invus transaction and FOR the amendment to our certificate of incorporation.

**Voting by Proxy**

Voting instructions are included on your proxy card. If you properly give your proxy and submit it to us in time to vote, one of the individuals named as your proxy will vote your shares as you have specified at the special meeting, or at any adjournment or postponement thereof. You may specify that your shares be voted for or against a proposal submitted at the meeting or that you are abstaining from voting for a proposal. If no specification is made, the shares will be voted for the Invus transaction and the amendment to our certificate of incorporation. Abstentions and broker non-votes will have the same effect as votes against the amendment to our certificate of incorporation. Abstentions and broker non-votes will not be treated as votes cast and have no effect on the outcome of the vote on the Invus transaction.

**How to Vote by Proxy**

By Telephone Or Internet.\* Call toll-free 1-866-540-5760 and follow the instructions. You will need to give the control number contained on your proxy card.

\* If you hold shares through a broker or other custodian, please follow the voting instructions for the voting form used by that firm.

Or go to [www.proxyvoting.com/lrx](http://www.proxyvoting.com/lrx) and follow the instructions. You will need to give the control number contained on your proxy card.

*In Writing.* Complete, sign, date and return your proxy card in the enclosed envelope.

**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 special 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 special meeting.

**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 proxy solicitation 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 solicitation materials to the beneficial owners of our shares, and we will reimburse them for their reasonable out-of-pocket expenses for forwarding such materials.

We have retained Innisfree M&A Incorporated, a proxy solicitation firm, to assist us in the solicitation of proxies for the special meeting. Innisfree and our directors, officers and employees may solicit proxies by mail, in person or by telephone or other electronic communication. We have agreed to pay Innisfree a fee of approximately \$25,000 and to reimburse its out-of-pocket expenses incurred in connection with its services. 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.

**Adjournments and Postponements**

Although it is not expected, the special meeting may be adjourned or postponed for the purpose of soliciting additional proxies. Any adjournment or postponement may be made without notice, other than by announcement made at the special meeting, by approval of the holders of a majority of the outstanding shares of our common stock present in person or represented by proxy at the special meeting, whether or not a quorum exists. Any signed proxies received by us prior to the special meeting will be voted in favor of an adjournment or postponement in these circumstances. Any adjournment or postponement of the special meeting for the purpose of soliciting additional proxies will allow those of our stockholders who have already sent in their proxies to revoke them at any time prior to their use.

## PROPOSAL ONE — THE INVUS TRANSACTION

### The Parties

*Lexicon Pharmaceuticals, Inc.* Lexicon Pharmaceuticals, Inc. is a biopharmaceutical company focused on the discovery and development of breakthrough treatments for human disease. We currently have clinical programs underway for such areas of major unmet medical need as irritable bowel syndrome and cognitive disorders. We have used our proprietary gene knockout technology to discover more than 100 promising drug targets and create an extensive pipeline of clinical and preclinical programs in the therapeutic areas of diabetes and obesity, cardiovascular disease, psychiatric and neurological disorders, cancer, immune system disorders and ophthalmic disease. To advance the development and commercialization of our programs, we are working both independently and through collaborators including Bristol-Myers Squibb Company, Genentech, Inc., N.V. Organon and Takeda Pharmaceutical Company Limited.

*The Invus Group, LLC.* The Invus Group, LLC is a New York-based investment firm with additional offices in London and Paris. Invus invests in a variety of equity transactions, including buyouts, longer term public equity investments, venture capital, and expansion financings. The Invus Group and its affiliates manage in excess of \$4 billion of capital in a broad range of industries, including consumer goods, consumer services, biotechnology, medical devices, education and software.

### Purpose and Background of the Invus Transaction

Over the course of the past nine months, we have realigned our operations to focus on drug discovery and development activities related to our 10T010 program, an ongoing initiative with the goal of advancing ten drug candidates into human clinical trials by the end of 2010. To date, we have initiated clinical trials for two drug candidates, with drug candidates from two additional programs in preclinical development and a substantial number of additional programs in various stages of preclinical research.

This operational realignment has been made possible by the scheduled completion of our Genome5000™ program, in which we are using our gene knockout and evaluative technologies to discover the physiological and behavioral functions of 5,000 human genes through analysis of the corresponding mouse knockout models. In this realignment, we have reduced the financial and human resources applied to our genetic research efforts and are reallocating those resources to our new drug development programs.

Both before and during this same period, our management and board of directors have been evaluating a variety of means to finance our operations, including additional drug discovery and development alliances, target validation collaborations, government grants and contracts, and technology licenses, as well as project financing arrangements and additional investments in our capital stock. In connection with such efforts, representatives of our management have held discussions with current and prospective collaborators and investors, including The Invus Group, an affiliate of which has been a stockholder since January 2004.

In April 2007, the president of The Invus Group notified our president and chief executive officer that Invus would be prepared to explore a possible substantial equity investment in us. On April 18, 2007, our representatives met with members of The Invus Group to discuss our business and financing strategy. In the course of such meeting, we and representatives of Invus also discussed how the availability of additional investment capital might affect that strategy, particularly with respect to the stage of development to which we would advance programs before entering into development and marketing collaborations with third parties in order to improve the proportion of the value of such programs retained by us and our stockholders. In the meeting, Invus' representatives expressed an interest in exploring an equity investment if it were of a size sufficient, in their view, to enable us to pursue a business strategy of progressing our programs to a more advanced stage of development before entering into development and marketing collaborations with third parties.

At a regularly scheduled board of directors' meeting on April 24 and 25, 2007, representatives of our management and the members of our board of directors discussed Invus' interest in a potential equity

investment, and the nature and status of discussions between the parties. Our board of directors authorized continued exploratory discussions with Invus regarding a potential proposal.

On April 30, 2007 and again on May 4, 2007, our president and chief executive officer and a representative of Morgan Stanley met with the president of The Invus Group to explore the potential nature and structure of a possible financing transaction. The parties agreed to proceed with further discussions following additional diligence by Invus regarding our business and operations.

On May 9, 2007, our representatives met with representatives of The Invus Group to discuss our small molecule drug discovery and medicinal chemistry capabilities.

On May 15 and 16, 2007, our representatives met with representatives of The Invus Group to discuss our drug discovery and development programs, our drug discovery and development capabilities, and our intellectual property strategy, and to further discuss our business and financing strategy.

On May 22, 2007, representatives of our management, including legal counsel, and a representative of Morgan Stanley met with representatives of Invus and its legal counsel to further explore the potential nature and structure of a possible financing transaction. Representatives of our management, including legal counsel, continued exploratory discussions with Invus and its legal counsel over the remainder of the week, and also engaged in discussions over the same period with members of our board of directors and its outside legal counsel regarding the nature and status of such discussions. Invus submitted a preliminary, non-binding proposal for consideration by our board of directors on May 25, 2007. Representatives of our management, including legal counsel, held discussions regarding the preliminary proposal over the course of the following three days with Invus, Invus' legal counsel, members of our board of directors, and the board's outside counsel.

At a board of directors' meeting held on May 29 and 30, 2007, representatives of our management, including legal counsel, and the members of our board of directors discussed the terms proposed by Invus and the nature of the discussions. During the portion of the meeting held on May 30, 2007, representatives of our management, including legal counsel, our board of directors, the board's outside counsel, and representatives of Morgan Stanley met to consider the Invus' proposal. Our board of directors considered, among other things, our business strategy, our financing strategy and needs, and alternatives to the proposal, including alternative financing transactions and potential strategic transactions, and Morgan Stanley's advice regarding the risks and benefits of, and likelihood of successfully completing, such a transaction or transactions relative to the transaction proposed by Invus. Among the benefits of Invus' proposal considered by our board of directors were (a) the substantial premium to market value represented by the blended price to be paid by Invus in the initial investment, (b) the financial flexibility that would be made available to us resulting from the proposed transaction, enabling us, among other things, to pursue a business strategy of progressing our programs to a more advanced stage of development before entering into development and marketing collaborations with third parties, and (c) the expectation that this business strategy, together with our greater financial resources, would improve our ability to negotiate more favorable collaborations and alliances, and would result in long-term benefits to our stockholders. Our board of directors also considered, among other things, (i) the influence that could be exercised by Invus, as a significant stockholder, (ii) the ability of Invus, within a specified range, to set the price at which common stock would be offered to our stockholders in a rights offering, and (iii) the possibility that, depending on the participation of other stockholders in any rights offering, Invus might acquire shares in a rights offering resulting in its possession of a majority of the voting power of our common stock, as well as the circumstances under which such possibility might be more or less likely to occur. At the conclusion of the meeting, our board of directors authorized continued negotiations with Invus regarding the proposed transaction.

On May 30, 2007, representatives of our management, including legal counsel, and a representative of Morgan Stanley met with representatives of Invus to engage in further discussions regarding the proposal. Further discussions continued the following day. At a board of directors' meeting held on June 1, 2007, representatives of our management, including legal counsel, our board of directors, the board's outside legal counsel, and representatives of Morgan Stanley met to consider Invus' proposal as revised following such discussions.

Further negotiations followed between Invus and its legal counsel and representatives of our management, including legal counsel, with involvement of our outside legal counsel, the board's outside legal counsel, and representatives of Morgan Stanley. At a board of directors' meeting held on June 14, 2007, representatives of our management, including legal counsel, our outside legal counsel, our board of directors, the board's outside legal counsel, and representatives of Morgan Stanley met to discuss the status of the negotiations and the terms and conditions of then-current drafts of definitive agreements outlining the proposed transaction. At a board of directors' meeting held on June 16, 2007, representatives of our management, including legal counsel, our outside legal counsel, our board of directors, the board's outside legal counsel, and representatives of Morgan Stanley met to consider the transaction proposed by Invus and review the terms and conditions of the final forms of definitive agreements for the transaction. After an extensive discussion of the terms and conditions of the relevant agreements, a review of the benefits and risks associated with the proposed transaction and the absence of more favorable financing, and the receipt of the advice of Morgan Stanley regarding the transaction and its oral opinion to the effect that, as of June 16, 2007 and based upon the factors and subject to the assumptions set forth in its opinion, the consideration to be received by us in connection with the initial investment pursuant to the securities purchase agreement was fair from a financial point of view to us, our board of directors unanimously approved the Invus transaction and the related agreements, the amendment to our certificate of incorporation and certain related matters. Following such approval, we entered into the securities purchase agreement, the warrant agreement, the registration rights agreement and the stockholders' agreement with Invus, effective June 17, 2007.

#### **Recommendation of our Board of Directors**

**Our board of directors has unanimously approved the Invus transaction and determined that the Invus transaction is advisable and in the best interest of our stockholders and unanimously recommends that our stockholders vote for its approval.**

Prior to approving the Invus transaction, our board of directors considered various alternatives to the Invus transaction. In approving the Invus transaction, our board of directors concluded that the Invus transaction presented the best course of action for us at this time. Our board of directors decided not to pursue the other alternatives considered. These alternatives would likely have been to the exclusion of Invus' proposal without any assurance that a better offer or transaction could be realized.

The material factors considered by our board of directors in making such recommendation include the following:

- the fairness of the price to be received by us;
- the opinion of Morgan Stanley that, as of June 16, 2007, and based upon the factors and subject to the assumptions set forth in its written opinion, the consideration to be received by us in connection with the initial investment pursuant to the securities purchase agreement was fair from a financial point of view to us;
- the substantial premium to market value represented by the blended price to be paid by Invus in the initial investment;
- our need for additional capital; and
- the financial flexibility made available to us as a result of the Invus transaction which will, among other things, enable us to implement a long-term financial strategy that will fund our extensive drug discovery and development pipeline and provide a foundation upon which we can build an integrated biopharmaceutical company.

#### **Opinion of Morgan Stanley**

Our board of directors retained Morgan Stanley to provide it with financial advisory services and a financial opinion in connection with the initial investment. Our board of directors selected Morgan Stanley to act as its financial advisor based on Morgan Stanley's qualifications, expertise, reputation and its knowledge of

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our business and affairs. At the meeting of our board of directors held on June 16, 2007, Morgan Stanley rendered its oral opinion to our board of directors, subsequently confirmed in writing, that as of June 16, 2007, and based upon the factors and subject to the assumptions set forth in its opinion, the consideration to be received by us in connection with the initial investment pursuant to the securities purchase agreement was fair from a financial point of view to us.

The full text of Morgan Stanley's opinion, dated as of June 16, 2007, which sets forth, among other things, the assumptions made, procedures followed, matters considered and limitations on the review undertaken by Morgan Stanley is attached as Annex B hereto. We urge you to read this opinion carefully and in its entirety. Morgan Stanley's opinion is directed to our board of directors, addresses only the fairness from a financial point of view of the initial investment pursuant to the securities purchase agreement, and does not address any other aspect of the offer or constitute a recommendation to any holder of our common stock or as to how holders of our common stock should vote at any stockholders' meeting held in connection with the transaction. The summary of the opinion of Morgan Stanley set forth in this proxy statement is qualified in its entirety by reference to the full text of the opinion.

In connection with rendering its opinion, Morgan Stanley, among other things:

- reviewed certain publicly available financial statements and other business and financial information about us;
- reviewed certain internal financial statements and other financial and operating data about us prepared by our management;
- reviewed certain financial projections prepared by our management;
- discussed our past and current operations and financial condition and our prospects with certain of our senior executives;
- reviewed the reported prices and trading activity for our common stock;
- compared the prices and trading activity of our common stock with that of certain other comparable publicly-traded companies and their securities;
- reviewed the financial terms, to the extent publicly available, of certain comparable acquisition transactions;
- participated in discussions and negotiations among our representatives and representatives of Invus;
- reviewed the securities purchase agreement, the registration rights agreement, the warrant agreement, and the stockholders' agreement;
- performed such other analyses and reviewed such other information and considered such other factors as Morgan Stanley deemed appropriate.

Morgan Stanley assumed and relied upon, without independent verification, the accuracy and completeness of the information supplied or otherwise made available to it by us for the purposes of its opinion. With respect to the financial projections, Morgan Stanley assumed that they had been reasonably prepared on bases reflecting the best currently available estimates and judgments of our future financial performance. In addition, Morgan Stanley assumed that the initial investment will be consummated in accordance with the terms set forth in the securities purchase agreement without any waiver, amendment or delay of any terms or conditions. Morgan Stanley are not legal, tax or regulatory advisors. They are financial advisors only and relied upon, without independent verification, our assessment and that of our legal, tax or regulatory advisors with respect to legal, tax and regulatory matters. Morgan Stanley did not make any independent valuation or appraisal of our assets or liabilities, nor was Morgan Stanley furnished with any such appraisals. Morgan Stanley's opinion is necessarily based on financial, economic, market and other conditions as in effect on, and the information made available to Morgan Stanley as of, June 16, 2007.

The following is a summary of the material financial analyses performed by Morgan Stanley in connection with its opinion. These summaries of financial analyses include information presented in tabular

format. In order to fully understand the financial analyses used by Morgan Stanley, the tables must be read together with the text of each summary. The tables alone do not constitute a complete description of the financial analyses.

*Historical Share Price Performance.* Morgan Stanley observed that the high and low trading prices in the 52 weeks prior to June 15, 2007 were \$4.79 and \$2.91, respectively.

*Securities Research Analysts' Future Price Targets.* Morgan Stanley reviewed the twelve-month public market trading price targets for our common stock prepared and published by securities research analysts during the period from May 1, 2007 to May 14, 2007. These targets reflected each analyst's estimate of the future public market trading price of our common stock. These price targets were as follows: \$5.00, \$6.00, \$6.00, \$7.00 and \$24.00. Using an equity cost of capital of 9.5%, Morgan Stanley discounted the analysts' price targets back twelve months to arrive at a range of present values of these price targets. The resulting present values for such price targets ranged from approximately \$4.57 to \$21.92.

The public market trading price targets published by securities research analysts do not necessarily reflect current market trading prices for our common stock and these estimates are subject to uncertainties, including our future financial performance and future financial market conditions.

*Discounted Cash Flow Analysis.* Morgan Stanley performed discounted cash flow analyses to determine a range of present values for our common stock based on financial projections prepared by our management. Morgan Stanley also analyzed additional scenarios that reflected various sensitivities on assumptions of our product peak sales, operating margin and product associated research and development. In calculating the discounted cash flow equity value per share, Morgan Stanley calculated the unlevered free cash flow estimates for a projection period from 2007 to 2031. The unlevered free cash flows were then discounted to present values as of June 30, 2007 using discount rates of 8.5% to 10.5%. Cash flows in all scenarios were probability-weighted to account for development risk in each clinical trial stage and regulatory approval risk. Under the "standalone case," which assumed that the initial investment was not made, it was assumed that most pipeline products currently being developed without the use of a development partner would be licensed after Phase 1 clinical trials, with us receiving royalties on sales of such products. In the standalone case, Morgan Stanley observed equity values of between approximately \$4.21 and \$5.89 per share. Assuming future dilution due to our standalone funding requirements, Morgan Stanley observed that the equity value per share to current stockholders was approximately \$1.99 to \$2.79. Under the "Invus case," which assumed completion of the initial investment, it was assumed that most current unlicensed pipeline products would be licensed after Phase 2a clinical trials, with us sharing in 50% of the operating profits of such products. In this scenario, Morgan Stanley observed equity values of between approximately \$7.46 and \$10.26 per share. Also under the Invus case, assuming future dilution due to completion of the rights offerings pursuant to the securities purchase agreement, Morgan Stanley observed equity value per share to current stockholders of between \$3.02 and \$4.16. Morgan Stanley noted that the equity value per share to current stockholders was greater in the initial investment scenario than the scenario in which the initial investment was not made.

*Analysis of Selected Transactions.* Using publicly available information, Morgan Stanley reviewed the terms of certain announced, pending, and completed biotechnology and pharmaceutical acquisition transactions; its review focused on, among other acquisition transactions:

<u>Acquiror</u>	<u>Target</u>
Genzyme Corporation	AnorMED, Inc.
Novartis Pharma AG	Neutec Pharma plc
Merck & Co., Inc.	Sirna Therapeutics, Inc.
Pfizer, Inc.	Vicuron Pharmaceuticals, Inc.
AstraZeneca plc	Cambridge Antibody Technology Group plc
Pfizer, Inc.	Esperion Therapeutics, Inc.
Amgen, Inc.	Abgenix, Inc.
AstraZeneca plc	MedImmune, Inc.
Eli Lilly & Co.	Applied Molecular Evolution, Inc.
Gilead Sciences, Inc.	Myogen, Inc.
Genzyme Corporation	Bioenvision, Inc.
Glaxosmithkline plc	Corixa Corporation
Amgen, Inc.	Tularik, Inc.
OSI Pharmaceuticals, Inc.	Eyetech Pharmaceuticals, Inc.
Genzyme Corporation	Bone Care International, Inc.
QLT, Inc.	Atrix Laboratories, Inc.
Genentech, Inc.	Tanox, Inc.
Chiron Corporation	PowderJect Pharmaceuticals plc
Novartis AG	Chiron Corporation
UCB SA	Celltech Group plc
Genzyme Corporation	ILEX Oncology, Inc.
Shire plc	Transkaryotic Therapies, Inc.
Actelion Ltd.	CoTherix, Inc.
Eli Lilly & Co.	ICOS Corporation
Glaxosmithkline plc	ID Biomedical Corporation
Allergan, Inc.	INAMED Corporation
Shire plc	New River Pharmaceuticals, Inc.

For each of the transactions above, Morgan Stanley reviewed the price paid for the acquired company and calculated the respective premiums to the acquired company's unaffected stock price one day prior to announcement of the transaction:

	<u>Mean</u>	<u>Median</u>
Premium Paid to One Day Prior Stock Price	48%	43%

Morgan Stanley applied a premium range of 30%-60% to the price of our common stock. These results yielded implied equity values per share for our common stock of between approximately \$4.00 and \$4.93. Morgan Stanley noted that the initial investment does not represent a change-in-control transaction, and thus the analysis of the selected transactions listed above, each of which did involve a change in control, was provided for indicative purposes only. The selected transaction analysis resulted in values which reflected a change-in-control premium and are not necessarily comparable to the values to be paid in a financing transaction not involving a change in control.

No company or transaction utilized in the transactions analyses is identical to us or the Invus transaction. In evaluating the transactions and peer groups, Morgan Stanley made judgments and assumptions with regard to industry performance, business, economic, market and financial conditions and other matters, many of which are beyond our control, such as the impact of competition on our business or the industries in which we are principally engaged, the growth of these industries and the absence of any material adverse change in our financial condition and prospects or the industries in which we are principally engaged or in the financial markets in general. Mathematical analysis, such as determining the mean or median, or the high or the low, is not in itself a meaningful method of using peer group data.



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In connection with the review of the initial investment by our board of directors, Morgan Stanley performed a variety of financial and comparative analyses for purposes of rendering its opinion. The preparation of a financial opinion is a complex process and is not necessarily susceptible to partial analysis or summary description. In arriving at its opinion, Morgan Stanley considered the results of all of its analyses as a whole and did not attribute any particular weight to any analysis or factor considered by it. Furthermore, Morgan Stanley believes that the summary provided and the analyses described above must be considered as a whole and that selecting any portion of its analyses, without considering all analyses, would create an incomplete view of the process underlying its analyses and opinion. In addition, Morgan Stanley may have given various analyses and factors more or less weight than other analyses and factors, and may have deemed various assumptions more or less probable than other assumptions, so that the ranges of valuations resulting from any particular analysis described above should not be taken to be Morgan Stanley's view of our actual value.

In performing its analyses, Morgan Stanley made numerous assumptions with respect to industry performance, general business and economic conditions and other matters, many of which are beyond our control. Any estimates contained in Morgan Stanley's analyses are not necessarily indicative of future results or actual values, which may be significantly more or less favorable than those suggested by such estimates. The analyses performed were prepared solely as part of Morgan Stanley's analysis of the fairness from a financial point of view of the consideration to be received by us in connection with the initial investment pursuant to the securities purchase agreement in connection with the delivery by Morgan Stanley of its opinion dated June 16, 2007 to our board of directors. The analyses do not purport to be appraisals or to reflect the prices at which our common stock might actually trade. In arriving at its opinion, Morgan Stanley was not authorized to solicit, and did not solicit, interest from any party with respect to an acquisition, business combination or other extraordinary transaction, involving us or any of our assets, nor did it negotiate with any party other than Invus. Additionally, Morgan Stanley's financial analysis related solely to the initial investment and did not address the relative merits of the initial investment as compared to any other alternative business transaction, or other alternatives, or whether or not such alternatives could be achieved or are available, including, without limitation, any transaction involving a sale, merger or similar transaction involving all of our equity or assets. Morgan Stanley also noted that the initial investment does not represent a change-in-control transaction.

Morgan Stanley's opinion was one of many factors taken into consideration by our board of directors in making its decision to approve the initial investment. Consequently, the Morgan Stanley analyses as described above should not be viewed as determinative of the opinion of our board of directors with respect to the value of our common stock, the initial investment consideration or of whether our board of directors would have been willing to agree to a different investment transaction.

Morgan Stanley is an internationally recognized investment banking and advisory firm. Morgan Stanley, as part of its investment banking and financial advisory business, is continuously engaged in the valuation of businesses and securities in connection with mergers and acquisitions, negotiated underwritings, competitive biddings, secondary distributions of listed and unlisted securities, private placements and valuations for corporate and other purposes. In the ordinary course of Morgan Stanley's trading and brokerage, investment management and financing activities, Morgan Stanley or its affiliates may at any time hold long or short positions, trade or otherwise effect transactions, for its own account or for the account of customers, in our equity or debt securities or loans. In the past, Morgan Stanley and its affiliates have provided us with financial advisory services and have received fees for the rendering of these services.

Pursuant to an engagement letter dated June 16, 2007, Morgan Stanley provided financial advisory services and a financial opinion in connection with the initial investment, and we agreed to pay Morgan Stanley a fee of three percent of the aggregate value of the consideration received by us upon the completion of the initial investment and the exercise by Invus of any warrants, which if the initial investment is completed will total approximately \$6.2 million. The fee is payable upon the earlier to occur of the purchase of shares of our common stock pursuant to an exercise by Invus of its warrants or the completion of the initial investment. We have also agreed to reimburse Morgan Stanley for its expenses incurred in performing its services. In addition, we have agreed to indemnify Morgan Stanley and its affiliates, their respective directors, officers,

agents and employees and each person, if any, controlling Morgan Stanley or any of its affiliates against certain liabilities and expenses, including certain liabilities under the federal securities laws, related to or arising out of Morgan Stanley's engagement and any related transactions.

#### **Interests of Certain Persons in the Invus Transaction**

In considering the recommendations of our board of directors with respect to the Invus transaction and the amendment to our certificate of incorporation, our stockholders should be aware that certain of our executive officers may have interests in the Invus transaction 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 approving the Invus transaction.

*Increase in Potential Payments upon Termination.* We are party to agreements with certain of our executive officers which provide for increased potential severance compensation in the event we undergo a "change in control" as this term is defined under those agreements. These agreements were generally entered into upon commencement of the executive officer's employment with us or before our April 2000 initial public offering, and have not been changed or modified in connection with the Invus transaction. The closing of the initial investment of the Invus transaction will be deemed a "change in control" under those agreements for certain executive officers and will result in increased severance compensation paid by us to those individuals if the employment of such executives were to be terminated without "cause" or by the executive for "good reason," as those terms as defined in the executive's agreement, or under certain other circumstances. Generally this increased compensation will take the form of a single sum payment of all, or some percentage of, the executive's target bonus for the year in which the termination occurs and/or an increase in the number of months' salary that will be paid after the executive's employment is terminated.

If the employment of Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, is terminated under circumstances that would entitle him to a severance payment under his employment agreement with us, he would be entitled to an additional single payment equal to his full target bonus due to the prior occurrence of a "change of control."

If the employment of any of our other executive officers is terminated under circumstances that would entitle the executive to a severance payment under such executive's agreement with us, generally the executive would be entitled to an additional single payment equal to 50% of such executive's target bonus and an additional six months of salary due to the prior occurrence of a "change of control." The details of our employment agreements with Dr. Sands, Julia P. Gregory, our executive vice president and chief financial officer, and our three other most highly compensated executive officers for the year ended December 31, 2006 are outlined in the proxy statement for our 2007 annual meeting under the section entitled "Executive and Director Compensation — Potential Payments upon Termination or Change in Control."

*Waiver of Accelerated Vesting of Stock Options.* Our stock option agreements with our executive officers provide for accelerated vesting of unvested stock options upon a "change in control" of the company. In connection with the Invus transaction, our executive officers have executed certain letter agreements pursuant to which the Invus transaction will not cause accelerated vesting of their stock options under the applicable stock option plans and agreements, to the extent the Invus transaction does not result in Invus owning in excess of 50% of the combined voting power of our then-outstanding voting securities.

#### **Use of Proceeds**

We currently intend to use the net proceeds from the Invus transaction to help fund our drug discovery and development pipeline and further our strategic goal of transitioning into an integrated biopharmaceutical company. Our currently planned operations are focused on drug discovery and development activities related

to our 10T010 program, an ongoing initiative with the goal of advancing ten drug candidates into human clinical trials by the end of 2010. Currently planned activities in support of our 10T010 program include:

- the scheduled completion of our Genome5000™ program, in which we are using our gene knockout and evaluative technologies to discover the physiological and behavioral functions of 5,000 human genes;
- the continued expansion of our medicinal chemistry, biotherapeutics and preclinical research activities to identify potential new drug candidates; and
- the initiation and conduct of preclinical development activities and human clinical trials for new drug candidates selected as a result of such efforts, as well as continued preclinical development activities and human clinical trials for our drug candidates that are already in development.

We expect to receive approximately \$198 million in net proceeds from the initial investment of the Invus transaction after deducting estimated fees and expenses of \$7.5 million incurred in connection with the initial investment. We currently anticipate that we will apply these net proceeds as follows:

- approximately \$20 to \$25 million to fund our research activities relating to the discovery and validation of drug targets in and resulting from our Genome5000 program;
- approximately \$70 to \$85 million to fund our research activities relating to the discovery and preclinical research of potential drug candidates for targets identified as a result of our target discovery and validation activities;
- approximately \$35 to \$70 million to fund preclinical development and human clinical trials of drug candidates selected from our drug discovery and preclinical research efforts;
- approximately \$30 to \$40 million to fund general and administrative expenses in support of the foregoing research and development efforts; and
- approximately \$5 to \$10 million to fund capital expenditures in support of the foregoing research and development efforts.

As of the date of this proxy statement, we cannot predict with certainty all of the particular uses for the proceeds from the initial investment, or the amounts that we will actually spend on the uses set forth above. The amounts and timing of our actual expenditures will depend upon numerous factors, including the progress of our research, development, and commercialization efforts, the progress of our clinical trials, and our operating costs and expenditures. The foregoing amounts exclude expenditures to be reimbursed by Symphony Icon, Inc., which has committed to fund up to \$45 million of the costs of our development of LX6171, LX1031 and LX1032, and our other existing collaborators. The amounts and timing of our use of the proceeds of the initial investment will likewise be dependent on future collaborations and alliances that we may enter, in which our collaborators may, among other things, bear all or a portion of the costs of our research or development activities relating to the programs included in the collaboration or alliance. Accordingly, our management will retain broad discretion in the allocation of net proceeds from the initial investment.

#### **Effects of the Invus Transaction on Stockholders**

Pursuant to the securities purchase agreement, Invus will purchase approximately 50.8 million shares of our common stock for approximately \$205 million in the initial investment. At the conclusion of the initial investment, Invus will own 40% of the outstanding shares of our common stock. Additionally, Invus will be given the right to require us to make two separate pro rata offerings of non-transferable rights to acquire common stock to all of our stockholders in an aggregated amount to be, subject to certain limitations, determined by Invus. In both offerings Invus will be required to purchase the entire portion of the rights offerings not subscribed for by other stockholders. Such offerings could increase Invus' percentage ownership of our outstanding shares above 40%. For additional information relating to the beneficial ownership of our common stock following the completion of the Invus transaction, see "Security Ownership of Certain Beneficial Owners and Management."

Stockholders should consider the following factors which may affect them, as well as the other information contained in this proxy statement, in evaluating the proposal to approve the Invus transaction.

*Possible Effect on Market Price of Our Common Stock.* We are unable to predict the potential effects of the Invus transaction on the trading activity and the market price of our common stock. In connection with the stockholders' agreement, we have granted Invus demand and piggyback registration rights in connection with the resale of the shares to be issued to Invus in the Invus transaction. See "— Registration Rights Agreement." These registration rights would facilitate the resale of Invus' shares into the public market, and any resale of these shares would increase the number of shares of our common stock available for public trading. Sales by Invus of a substantial number of shares of our common stock in the public market, or the perception that such sales might occur, could have a material adverse effect on the price of our common stock.

*Invus will be a Significant Stockholder.* Upon the completion of the initial investment, Invus will beneficially own 40% of our outstanding common stock, and will be our largest stockholder. As a significant stockholder, Invus will be able to significantly influence matters submitted to our stockholders for a vote. Pursuant to the stockholders' agreement, Invus has certain rights, including the right to designate members of our board of directors, preemptive rights in connection with future equity issuances by us, and consent rights over certain types of actions by us. See "— Stockholders' Agreement." In addition, any rights offerings could increase Invus' percentage of ownership of our outstanding shares. Depending upon the participation of other stockholders in any rights offering, Invus might acquire shares sufficient to result in Invus' possession of a majority of the voting power of our common stock.

*Expansion of our Board of Directors.* At the closing of the initial investment, our board of directors will be expanded to provide for eleven members, three of whom will be designated by Invus.

*Dilution.* The Invus transaction will have a substantial dilutive effect on a stockholder's percentage voting power. The issuance may have a dilutive effect on future earnings per share.

#### **Securities Purchase Agreement**

*Initial Investment.* In the initial investment, Invus will purchase shares of our common stock for a total of approximately \$205 million in two parts as follows:

(a) a number of shares of our common stock that, when added to the shares of our common stock already owned by Invus and its affiliates (including the 3,891,108 shares owned by an affiliate of Invus on the date of the securities purchase agreement and any shares issued upon exercise of the warrants but excluding, for the avoidance of doubt, the shares of our common stock to be issued pursuant to clause (b) below), equals 19.9% of the aggregate number of shares of our common stock outstanding as of the closing of the initial investment (which is expected to be approximately 16.5 million shares) for a per share purchase price equal to \$3.0915; and

(b) a number of shares of our common stock that, when added to the number of shares of our common stock already owned by Invus and its affiliates and the number of shares subject to clause (a) above, equals 40% of the aggregate number of shares of our common stock outstanding as of the closing of the initial investment (which is expected to be approximately 34.3 million shares) for a per share purchase price equal to \$4.50.

*The Closing of the Initial Investment.* The closing of the initial investment will take place on the third business day after the satisfaction or waiver of the closing conditions set forth in the securities purchase agreement (other than those that by their terms are to be satisfied at the closing), unless another date is agreed to by Invus and us.

*First Rights Offering.* For a period of 90 days following the date (which we refer to as the first rights offering trigger date) which is 27 months after the closing of the initial investment, Invus will have the right to require us to make a pro rata offering of non-transferable rights to acquire shares of our common stock to all of our stockholders (which we refer to as the first rights offering) in an aggregate amount to be designated by Invus not to exceed an amount equal to (a) the quotient of (i) \$550 million, *minus* the amount of the initial

investment, *minus* the aggregate amount paid by Invus upon the exercise of any warrants, divided by (ii) two (which quotient is expected to be approximately \$172.5 million), *minus* (b) the aggregate net proceeds received in all qualified offerings (as defined below), if any, completed prior to the first rights offering trigger date. The price per share in the first rights offering would be designated by Invus in a range between \$4.50 and the average of the volume-weighted average trading prices of our common stock on the Nasdaq Stock Market for the ten full trading days immediately prior to the date on which Invus exercises its rights to require us to conduct the first rights offering. The first rights offering trigger date could be changed to as early as 24 months after the closing of the initial investment with the approval of Invus and the members of our board of directors who are not affiliated with Invus (which we refer to as the unaffiliated board). All stockholders who exercise their rights in the first offering would have oversubscription rights with respect to the first rights offering, and Invus would be required to purchase the entire portion of the first rights offering that is not subscribed for by other stockholders.

A "qualified offering" consists of a bona fide financing transaction comprised of, subject to certain restrictions, our issuance of shares of our common stock at a price greater than \$4.50 per share, which transaction is not entered into in connection with our entry into any other transaction (including, a collaboration or license for the discovery, development or commercialization of pharmaceutical products) involving the purchaser of such common stock.

*Second Rights Offering.* For a period of 90 days following the date (which we refer to as the second rights offering trigger date) which is 12 months after the later of (a) the first rights offering trigger date or (b) the date on which Invus exercised its right to require us to conduct the first rights offering, Invus would have the right to require us to make a pro rata offering of non-transferable rights to acquire shares of our common stock to all of our stockholders (which we refer to as the second rights offering) in an aggregate amount to be designated by Invus not to exceed an amount equal to \$550 million, *minus* the amount of the initial investment, *minus* the aggregate amount paid by Invus upon the exercise of any warrants, *minus* the amount of the first rights offering, *minus* the aggregate net proceeds received in all qualified offerings, if any, completed prior to the second rights offering trigger date. The price per share in the second rights offering would be designated by Invus in a range between \$4.50 and the average of the volume-weighted average trading prices of our common stock on the Nasdaq Stock Market for the ten full trading days immediately prior to the date on which Invus exercises its rights to require us to conduct the second rights offering. All stockholders who exercise their rights in the second rights offering would have oversubscription rights with respect to the second rights offering, and Invus would be required to purchase the entire portion of the second rights offering that is not subscribed for by other stockholders.

*Conduct of Business Pending the Closing.* We have agreed to restrictions on our activities between the date of the securities purchase agreement and the closing of the initial investment. In general, subject to certain exceptions, we are required to conduct our operations in the ordinary course of business consistent with past practice, to seek to preserve substantially intact our current business organization, to seek to keep available the service of our current officers, employees and consultants and to seek to preserve our relationships with customers, suppliers and others having significant business relations with us. Subject to certain exceptions, we have agreed to specific restrictions that prohibit us or our subsidiaries from taking the following actions without the prior written consent of Invus:

- amending our certificate of incorporation or by-laws;
- issuing, selling, pledging or otherwise disposing of or encumbering any of our stock or other equity interests or equity equivalents;
- selling, pledging or otherwise disposing of or encumbering any of our material property or assets;
- declaring, setting aside or paying any dividend or other distribution or payment to our stockholders or entering into any agreement with respect to the voting of our capital stock;
- splitting, combining, dividing or reclassifying any shares of our capital stock or other equity interests;
- redeeming, repurchasing or otherwise acquiring any of our capital stock or other equity interests;

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- acquiring any corporation, partnership, other business organization or any division thereof;
- incurring any indebtedness for borrowed money or issuing any debt securities or assuming or guaranteeing the obligations of any person, or making any loans or advances, or granting any security interest in, any of our assets except in the ordinary course of business;
- terminating or materially changing any material contract other than in the ordinary course of business;
- entering into any material contract other than in the ordinary course of business;
- making any capital expenditure or purchasing fixed assets in excess of \$500,000 in the aggregate other than as set forth in our capital expenditure plan;
- increasing the compensation of, granting severance rights to or entering into any employment or severance agreement with our or our subsidiaries' current or former directors or officers;
- establishing, adopting, entering into or amending any employee benefit plan or amending or waiving any performance or vesting criteria or accelerating the vesting, exercisability or funding under any employee benefit plan;
- pre-paying long-term debt or paying, discharging or satisfying any claims, liabilities or obligations except in the ordinary course of business;
- adopting or proposing to adopt or maintain any stockholders rights plans, "poison pill" or other similar plan or agreement unless Invus is exempted from such plan or agreement;
- modifying, amending, terminating, or releasing or assigning any material rights or claims with respect to any confidentiality or standstill agreement;
- taking any action to exempt or make not subject to the restrictions of Section 203 of the Delaware General Corporate Law or any other state takeover law, or state law that purports to limit or restrict business combinations or the ability to acquire or vote shares, persons or actions which would have otherwise been subject to the restrictive provisions thereof; and
- announcing an intention, entering into an agreement or otherwise making a commitment to do any of the foregoing.

*Restrictions on Issuances of Common Stock after the Closing.* In the event the initial investment is completed, until the later of the completion of the second rights offering or the expiration of the 90-day period following the second rights offering trigger date, we have agreed not to issue any of our common stock for a per share price of less than \$4.50 without the prior written consent of Invus, except pursuant to an employee or director stock option, incentive compensation or similar plan or to persons involved in the pharmaceutical industry in connection with simultaneous strategic transactions involving such persons in the ordinary course.

*Stockholders Meeting.* We have agreed to cause a special meeting of our stockholders to be called and held as soon as practicable for the purpose of voting on the approval of the Invus transaction and the amendment to our certificate of incorporation and to solicit proxies from our stockholders to obtain the requisite vote on these matters. We have also agreed that, subject to our board of directors' fiduciary duties in connection with a material development or change in circumstances occurring or arising after the date of the securities purchase agreement that was neither known to our board of directors nor reasonably foreseeable as of or prior to the date of the securities purchase agreement, our board of directors will recommend to our stockholders the approval of the Invus transaction and the amendment to our certificate of incorporation.

*No Solicitation.* As part of the securities purchase agreement we have agreed that, until the earlier of the closing of the initial investment or the termination of the securities purchase agreement, neither we nor any subsidiary nor any of our respective directors, officers, employees, agents or representatives, including any financial advisor, attorney or other advisor will, directly or indirectly:

- solicit, initiate or knowingly encourage or take any other action designed to result in or facilitate any significant investment in us by another person, any significant acquisition of shares of our common

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stock or any merger, reorganization, liquidation or other transaction that would be inconsistent with the Invus transaction (which we refer to as an alternative transaction);

- enter into, continue or otherwise participate in any discussions or negotiations regarding, or furnish to any person any information in connection with, or otherwise cooperate in any way with, any alternative transaction;
- approve, recommend or endorse, or enter into any agreement relating to, any alternative transaction; or
- waive, terminate, modify or fail to enforce any provision of any "standstill" or similar obligation of any person other than Invus.

However, at any time prior to obtaining stockholder approval for the Invus Transaction, in response to an unsolicited bona fide written alternative transaction, we may have discussions with and provide non-public information (so long as such information has been or is simultaneously provided to Invus) to a third party that has made such alternative transaction if:

- our board of directors determines in good faith after consulting with outside counsel and financial advisors and after taking into account any amendment to the securities purchase agreement or any other transaction proposed by Invus, that failing to take such action would result in a breach of the fiduciary duties of our board of directors under applicable law; and
- the third party executes a customary confidentiality agreement.

*Representations and Warranties.* The securities purchase agreement contains representations and warranties made by the parties. The representations and warranties made by us relate to:

- our and our subsidiaries' corporate existence, qualification to conduct business and corporate standing and power;
  - our ownership of subsidiaries;
  - our certificate of incorporation and by-laws and those of our subsidiaries;
  - our capitalization;
  - our corporate authority to enter into, and carry out the obligations under, the securities purchase agreement and related agreements and the enforceability of the securities purchase agreement and related agreements;
  - the absence of conflicts, the completion of required filings, and the obtaining of consents and approvals required to consummate the transactions contemplated by the securities purchase agreement;
  - our possession of permits necessary to operate our properties and carry on our business and compliance with laws;
  - clinical trials conducted by us;
  - our filings with the SEC;
  - our financial statements;
  - the absence of certain changes or events;
  - the absence of pending or threatened litigation;
  - employment and labor matters affecting us, including matters relating to our employee benefit plans;
  - our property and leases;
  - our intellectual property;
  - tax matters;
  - environmental matters;
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- our material contracts and debt instruments;
- our transactions with related parties;
- our insurance matters;
- our disclosure controls and internal controls over financial reporting;
- the absence of any sale of securities by us or our subsidiaries that would subject the offering, issuance or sales of the shares to be sold to Invus in the initial investment to the registration provisions of the Securities Act of 1933, as amended, or the Securities Act;
- the stockholder votes required for the approval of the Invus transaction and the amendment to our certificate of incorporation;
- the absence of the application of Section 203 of the General Corporation Law of Delaware or other state takeover laws to the Invus transaction;
- the receipt by us of the opinion of our financial advisor;
- the absence of undisclosed broker fees;
- the accuracy and completeness of information supplied by us in this proxy statement; and
- our board of directors' determination with respect to the independence of Invus' director designees.

Certain of our representations and warranties are qualified as to "materiality" or "material adverse effect." For purposes of the securities purchase agreement, "material adverse effect" with respect to us and our subsidiaries means any event, circumstance, change or effect that, either individually or combined with all other events, circumstances, changes or effects:

- has a material adverse effect on the business, operations, assets, liabilities (including contingent liabilities), condition (financial or otherwise) or results of operations of us and our subsidiaries, taken as a whole; or
- materially impairs our ability to consummate the Invus transaction and to perform our obligations under the securities purchase agreement.

A material adverse effect will not include any event, circumstance, change or effect to the extent arising out of:

- any events, circumstances, changes or effects occurring after the date of the securities purchase agreement that affect the biopharmaceutical industry generally to the extent not disproportionately impacting us and our subsidiaries; and
- any changes in general economic, legal, regulatory or political conditions occurring after the date of the securities purchase agreement to the extent not disproportionately affecting us and our subsidiaries.

The representations and warranties contained in the securities purchase agreement will be deemed to be made at the closing of the initial investment and the closing of each rights offering, if any, and, subject to certain exceptions, will survive for 12 months following each closing.

*Conditions.* The parties' respective obligations to complete the initial investment and the purchase and sale of shares of our common stock in each of the rights offerings are subject to the satisfaction or waiver of various conditions, the most significant of which are:

- with respect to the initial investment only, the approval of the Invus transaction and the amendment to our certificate of incorporation by our stockholders;
- the absence of any law, ordinance, regulation, rule, code, executive order, injunction, judgment, decree or other order prohibiting, restricting or otherwise preventing or making illegal the completion of the transactions contemplated by the securities purchase agreement;



- the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976;
- the absence of any pending or threatened action before any governmental authority wherein an unfavorable injunction, judgment, order, decree, ruling or charge, that would reasonably be expected to be adversely determined against us, Invus or our respective affiliates, would reasonably be expected to (a) prevent consummation of, or cause to be rescinded, any of the transactions contemplated by the securities purchase agreement or any related agreement or (b) materially adversely affect the rights and powers of Invus and its affiliates as a stockholder of ours;
- the representations and warranties of the other party contained in the securities purchase agreement and each related agreement that are qualified by materiality or material adverse effect being true and correct as of the date of the securities purchase agreement or the applicable rights offering trigger date and as of the closing of the initial investment and the closing for the applicable rights offering, and the representations and warranties that are not so qualified, being true and correct in all material respects; and
- the other party having performed or complied with its obligations and covenants contained in the securities purchase agreement in all material respects.

Additionally, Invus does not have to complete the Invus transaction unless:

- we have adopted resolutions to increase the number of directors comprising our board of directors from eight to eleven and taken action to cause the three persons designated by Invus to be elected or appointed to our board of directors; and
- the amendment to our certificate of incorporation has become effective.

*Termination.* The securities purchase agreement may be terminated in certain instances.

Either we or Invus may terminate the securities purchase agreement if:

- we and Invus mutually agree to terminate the securities purchase agreement;
- the closing of the initial investment does not occur on or before November 15, 2007, provided that the party seeking to terminate has not caused the delay of or prevented the occurrence of the closing of the initial investment;
- a governmental authority in the United States enacts, issues, promulgates, enforces or enters any final and nonappealable order, decree, judgment, injunction or ruling making the Invus transaction illegal or otherwise preventing or prohibiting the Invus transaction; or
- stockholder approval is not obtained upon a vote taken at the special meeting.

Invus may terminate the securities purchase agreement if:

- our board withdraws or changes its recommendation to the stockholders regarding the Invus transaction or the amendment to our certificate of incorporation;
- there is any event, development or change of circumstance that constitutes, has had or would reasonably be expected to have, individually or in the aggregate, a material adverse effect on us and it is not cured within 20 days after we receive written notice from Invus; or
- we have breached any representation, covenant or agreement set forth in the securities purchase agreement and such breach is not cured within 20 days after we receive written notice from Invus.

We may terminate the securities purchase agreement if:

- Invus breaches any representation, covenant or agreement set forth in the securities purchase agreement and such breach is not cured within 20 days after Invus receives written notice from us.

*Amendments and Waivers.* The securities purchase agreement may be amended at any time prior to the closing of the initial investment. However, after stockholder approval is obtained, no amendment requiring additional stockholder approval may become effective without the approval of the stockholders. All amendments to the securities purchase agreement must be in writing signed by each party.

Any party to the securities purchase agreement may (a) extend the time for performance of the other party, (b) waive any inaccuracy in the representations of the other party and (c) waive compliance with any agreement of the other party or condition to such party's obligations. All waivers must be in writing and signed by the party or parties to be bound thereby.

#### **Warrant Agreement**

*Issuance of Warrants.* Concurrently with the execution of the securities purchase agreement and pursuant to the warrant agreement, dated as of June 17, 2007, between us and Invus, we have issued to Invus warrants to purchase 16,498,353 shares of our common stock at an exercise price of \$3.0915. As indicated above, purchases of shares upon exercise of the warrants prior to the closing of the initial investment will reduce the number of shares to be purchased by Invus at the same price in the initial investment.

*Exercise Period of Warrants.* The period during which the warrants are exercisable began on the date of the warrant agreement and will expire at 5:00 p.m. New York time, on the date of the earliest to occur of:

- the closing of the initial investment;
- 30 business days after the special meeting held to vote on the Invus transaction and the amendment to our certificate of incorporation (so long as we have not materially breached the securities purchase agreement, our board of directors has not withdrawn or changed its recommendation that our stockholders vote in favor of the Invus transaction or the amendment to our certificate of incorporation and no acquisition proposal (as defined below) has been consummated, announced or made public or approved or recommended by our board of directors);
- three years following the termination of the securities purchase agreement, provided that the termination of the agreement has not been due to a material breach thereof by Invus;
- nine months after the stockholders meeting if, prior to the meeting, our board of directors has withdrawn or changed its recommendation that our stockholders vote in favor of the Invus transaction and the amendment to our certificate of incorporation or if an acquisition proposal has been consummated, announced or made public (so long as we have not materially breached the securities purchase agreement); and
- the termination of the securities purchase agreement if such agreement is terminated due to a material breach by Invus.

An "acquisition proposal" means any proposal to acquire (by purchase, exchange, merger or otherwise) assets or business constituting 20% or more of our revenues, net income or assets or 20% or more of any class of our equity securities.

*Effect of Tender or Exchange Offer on the Warrants; Anti-Dilution.* In the event that we purchase shares of our common stock pursuant to a tender offer or exchange offer for a price per share of our common stock that is greater than the then-current market value of the shares, we will be required to, within ten days of the expiry of such tender or exchange offer, purchase the warrants for a comparable consideration per share based on the number of shares which the warrant holders would receive upon exercise of the warrants. If the tender offer is made only for a portion of the outstanding shares we will be required to purchase shares issuable upon exercise of the warrants in the same pro rata proportion. We will not be required to make such an offer if the per share consideration is an amount less than the then-existing exercise price per share of the warrants. The exercise price of the warrants and the number of shares issuable upon the exercise of the warrants are subject to customary anti-dilution adjustments.

*Standstill and Furnishing of Information.* As part of the warrant agreement, Invus has agreed, subject to certain exceptions, that it will not, without the approval of our unaffiliated board, directly or indirectly:

- acquire beneficial ownership of any shares of our common stock other than upon the exercise of the warrants;
- solicit proxies to vote any of our voting securities or any voting securities of our subsidiaries;
- submit to our board of directors a written proposal for any merger, recapitalization, reorganization, business combination or other extraordinary transaction involving an acquisition of us or any of our subsidiaries or any of our or our subsidiaries' securities or assets by Invus and its affiliates;
- enter into discussions, negotiations, arrangements or understandings with any third party with respect to any of the foregoing; or
- request us or any of our representatives, directly or indirectly, to amend or waive any of these standstill provisions.

The standstill provisions of the warrant agreement will terminate on the earliest to occur of:

- the one-year anniversary of the first date on which any warrants have been exercised;
- the date on which the shares of our common stock beneficially owned by Invus and its affiliates represent less than 10% of the aggregate number of shares of our common stock then outstanding;
- the date on which any person consummates, announces or makes public any acquisition proposal or our board of directors approves or recommends, or proposes to approve or recommend, any acquisition proposal; or
- the closing of the initial investment.

Until such time as the standstill restrictions are in place, we have agreed to provide Invus such financial, management and operations plans, reports and information as exist and as are requested by Invus, and to afford Invus reasonable access to our and our subsidiaries' officers, employees, agents, properties, offices and other facilities, books and records as Invus may reasonably request.

#### **Registration Rights Agreement**

Concurrently with the execution of the securities purchase agreement, we entered into a registration rights agreement with Invus. Pursuant to the agreement, dated as of June 17, 2007, we have agreed to grant Invus certain registration rights related to the shares of our common stock to be acquired by Invus under the other agreements described in this proxy statement. These registration rights are transferable to any third party to whom Invus transfers a number of restricted shares of common stock that would result in such third party owning in excess of 3% of the total number of outstanding shares of our common stock.

*Demand Registrations.* Holders of such registration rights would have the rights to initiate (a) up to five demand registrations if the closing of the initial investment occurs, (b) up to three demand registrations if any of the warrants have been exercised, but the closing of the initial investment does not occur, and (c) an unlimited number of demand registrations if the number of shares of common stock owned by Invus and its permitted transferees at any time exceeds 50% of the total number of outstanding shares of our common stock. At the registration rights holder's request, any such demand registrations may also include a shelf registration.

We will not be required to effect more than one demand registration in any six month period. Also, we will not be required to effect a demand registration during the period commencing three months prior to the date on which Invus delivers to us a notice exercising its rights to require us to conduct a rights offering and ending on the closing of the applicable rights offering, or, if the applicable rights offering notice is not delivered, ninety days after the applicable rights offering trigger date.

*Piggyback Registrations.* Subject to certain exceptions, registration rights holders will have piggyback registration rights if at any time we propose to (i) file a registration statement under the Securities Act, with

respect to an offering by us for our own account or the account of any holders of any class of our common equity securities or (ii) effect an offering of stock pursuant to an effective shelf registration statement. We are required to give written notice of such proposed filing or offering as soon as practicable, but in no event less than 20 days before the anticipated filing date or the commencement of such offering, and give Invus and its permitted transferees the opportunity to include in such registration the shares of our common stock held by them on the same terms and conditions as any similar securities.

*Shelf Registration.* Registration rights holders will also have the right to cause the company to file with the SEC a shelf registration statement pursuant to Rule 415 under the Securities Act, but have agreed not to effect a public distribution of registrable securities pursuant to an effective shelf registration during the period commencing three months prior to the date on which Invus delivers to us a notice exercising its rights to require us to conduct a rights offering and ending on the closing of the applicable rights offering, or, if the applicable rights offering notice is not delivered, ninety days after the applicable rights offering trigger date.

*Holdback Agreement.* Registration rights holders will agree not to offer, sell or transfer any shares during the 14 days prior to, and during the 90-day period following, a public offering made pursuant to a registration statement filed under the Securities Act if requested in writing by the managing underwriters.

*Fees.* All fees and expenses (including reasonable fees and expenses of counsel) in connection with a registration will be paid by us, other than underwriting fees and discounts.

#### **Stockholders' Agreement**

*Changes in our Board of Directors.* Concurrently with the execution of the securities purchase agreement, we entered into a stockholders' agreement with Invus under which Invus will have the right to designate three members of our board of directors at the closing of the initial investment and, from and after the first anniversary of the closing of the initial investment, the right to designate the greater of three members or 30% (or the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates, if less than 30%) of all members of our board of directors, rounded up to the nearest whole number of directors. In the event that the number of shares of our common stock owned by Invus and its affiliates ever exceeds 50% of the total number of shares of our common stock then outstanding (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement), from and after that time, Invus will 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 (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement), rounded up to the nearest whole number of directors. From and after the closing of the initial investment, if requested by Invus, the directors appointed by Invus would have proportionate representation on the board of any subsidiary and on each committee of our board of directors and on the board of directors of any subsidiary, subject to the relevant requirements of the SEC and the Nasdaq Stock Market.

Invus' rights with respect to the designation of members of our board of directors, the boards of directors of any subsidiary and any of their respective 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 will also have the right to terminate these provisions at any time following the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus and its affiliates from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders' agreement).

*Preemptive Rights.* From and after the closing of the initial investment, Invus will have preemptive rights under the stockholders' agreement to participate in future equity issuances by us (including any qualified offering), 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 overallotment (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 the tenth anniversary of the closing of the initial investment 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%.

**Standstill Provisions.** From and after the closing of the initial investment, Invus will be subject to standstill provisions restricting its ability to purchase or otherwise acquire additional shares of common stock from third parties to an amount that would result in its ownership of our common stock not exceeding 49% of the total number of shares outstanding. These standstill provisions will not apply to the acquisitions of securities by way of stock splits, stock dividends, reclassifications, recapitalizations, or other distributions by us, acquisitions contemplated by the securities purchase agreement, the warrant agreement and the stockholders' agreement, including in the rights offerings and upon Invus' exercise of preemptive rights under the stockholders' agreement.

Except for acquisitions pursuant to the provisions described above, and subject to certain exceptions, Invus has agreed that it will not, and will cause its affiliates not to, without the approval of our unaffiliated board, directly or indirectly:

- solicit proxies to vote any of our voting securities or any voting securities of our subsidiaries;
- submit to our board of directors a written proposal for any merger, recapitalization, reorganization, business combination or other extraordinary transaction involving an acquisition of us or any of our subsidiaries or any of our or our subsidiaries' securities or assets by Invus and its affiliates;
- enter into discussions, negotiations, arrangements or understandings with any third party with respect to any of the foregoing; or
- request us or any of our representatives, directly or indirectly, to amend or waive any of these standstill provisions.

The standstill provisions of the stockholders' agreement will terminate on the earliest to occur of (a) the tenth anniversary of the closing of the initial investment, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all of the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement), (d) the date on which any third party makes a public proposal to acquire (by purchase, exchange, merger or otherwise) assets or business constituting 50% or more of our revenues, net income or assets or 50% of any class of our equity securities of our board of directors recommends or approves, or proposes to recommend or approve, any such transaction or (e) the date on which any third party acquires beneficial ownership (by purchase, exchange, merger or otherwise) of assets or business constituting 20% or more of our revenues, net income or assets or 20% of any class of our equity securities or our board of directors recommends or approves, or proposes to recommend or approve, any such transaction.

**Sales to Third Parties.** Subject to certain exceptions, Invus has agreed that neither it nor its affiliates will sell any shares of common stock to third parties that are not affiliated with Invus if, to Invus' knowledge, such transfer would result in any such third party (or any person or group including such third party) owning more than 14.9% of the total number of outstanding shares of our common stock.

The provisions of the stockholders' agreement relating to sales to third parties will terminate on the earliest to occur of (a) the tenth anniversary of the closing of the initial investment, (b) the date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates falls below

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10%, and (c) date on which the percentage of all the outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus and its affiliates from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders' agreement).

*Voting of Shares.* In any election of persons to serve on our board of directors occurring after the closing of the initial investment, Invus will be obligated to vote all of the shares of common stock held by it and its affiliates in favor of the directors nominated by our board of directors, as long as we have complied with our obligation with respect to the designation of members of our board of directors described above under the heading "— Changes in our Board of Directors" and the individuals designated by Invus for election to our board of directors have been nominated, and, if applicable, are serving on our board of directors. With respect to all other matters submitted to a vote of the holders of our common stock after the closing of the initial investment, Invus will be obligated to vote any shares that it acquired from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of common stock, as permitted by the standstill provisions of the stockholders' agreement, in the same proportion as all the votes cast by other holders of our common stock, unless Invus and we (acting with the approval of the unaffiliated board) agree otherwise. Invus may vote all other shares of our common stock held by it in its sole discretion.

The provisions of the stockholders' agreement relating to voting will terminate on the earliest to occur of (a) the tenth anniversary of the closing of the initial investment, (b) the date on which the percentage of all the outstanding shares of our common stock held by Invus and its affiliates falls below 10%, (c) the date on which the percentage of all outstanding shares of our common stock owned by Invus and its affiliates exceeds 50% (not counting for such purpose any shares acquired by Invus from third parties in excess of 40% (or, if higher, its then pro rata amount) of the total number of outstanding shares of our common stock, as permitted by the standstill provisions of the stockholders' agreement), and (d) the termination of the standstill provisions in accordance with the stockholders' agreement.

*Minority Protections.* From and after the closing of the initial investment, Invus will be entitled to certain minority protections, including consent rights over (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 or 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 minority protections will terminate on the earlier to occur of the tenth anniversary of the closing of the initial investment and the date on which Invus and its affiliates hold less than 15% of the total number of outstanding shares of our common stock.

*Information Rights.* We have agreed to furnish or make available to Invus, promptly after such information becomes available to us, (a) such annual budget, business plans and financial forecasts as are customarily provided to our board of directors, (b) following the end of each fiscal quarter or fiscal year, such consolidated financial statements and operations reports as are customarily provided to our board of directors, (c) following the end of each calendar month, such internal management financial and operations reports regarding our financial results and operations as are customarily provided to our senior management, (d) all information that is provided to members of our board of directors in their capacity as such, and (e) such other financial, management and operations reports reasonably requested by Invus. We have also agreed to afford Invus reasonable access to our and our subsidiaries' officers, employees, agents, properties, offices and other facilities, books and records as Invus may reasonably request.

**PROPOSAL TWO — AMENDMENT TO OUR CERTIFICATE OF INCORPORATION**

**Increase in Authorized Shares of our Common Stock**

We must increase the number of authorized shares of our common stock in order to have a sufficient number of authorized shares to issue in connection with the Invus transaction. Our board of directors believes that it is advisable to amend Article IV of our certificate of incorporation to increase the number of authorized shares of common stock from 120 million shares to 300 million.

As of July 19, 2007, of the 120 million shares of our common stock authorized by our certificate of incorporation, approximately 86 million shares were issued and outstanding and approximately 17.5 million shares were reserved for issuance under our stock incentive plans or upon exercise of warrants other than those issued to Invus. Approximately 16.5 million additional shares were reserved for issuance upon exercise of the warrants issued to Invus. If the initial investment is completed, approximately 50.8 million shares of our common stock will be issued to Invus, including shares, if any, issued upon exercise of the Invus warrants. After the proposed increase in the number of authorized shares of our common stock to 300 million and the initial investment, approximately 145.7 million shares of our common stock would be authorized, but unissued and not reserved for issuance.

In addition to allowing us to meet our obligations to issue stock under the securities purchase agreement, our board of directors believes that this amount of authorized common stock will provide us with greater flexibility in effecting future acquisitions and financings without the delay and expense associated with obtaining the approval or consent of our stockholders at the same time the shares are needed. We expect that our future growth may require the use of our common stock from time to time either as consideration for acquisitions or as part of a financing for us either through the use of our common stock or securities convertible into our common stock. Such shares may be issued in conjunction with both public offerings and private placements of shares of our common stock. Such shares could also be used for our stock-based compensation plans, subject to appropriate stockholder approval. Our stockholders other than Invus do not have any preemptive rights to purchase additional shares of our common stock. Other than the Invus transaction, we do not have any current plans, proposals or understandings that would require the use of the additional authorized shares of our common stock to be issued.

The text of the amendment to increase the number of authorized shares of our common stock from 120 million to 300 million can be found in the form of the second certificate of amendment to our restated certificate of incorporation, which is attached as Annex A to this proxy statement.

**Recommendation of our Board of Directors**

**Our board of directors has unanimously approved the amendment to our certificate of incorporation to increase the number of authorized shares of our common stock from 120 million to 300 million, has determined that this amendment to our certificate of incorporation is advisable and in the best interest of our stockholders and recommends that our stockholders vote for its approval.**

**Effects of the Amendment to our Certificate of Incorporation**

Stockholders should consider the following factors which may affect them, as well as the other information contained in this proxy statement, in evaluating the proposal to approve the amendment to our certificate of incorporation to increase our authorized shares of common stock.

*Possible Dilution from Future Issuance of Additional Shares.* We are seeking to amend our certificate of incorporation to increase the number of authorized shares of our common stock from 120 million to 300 million shares, and the interests of the holders of our common stock could be diluted substantially as a result. Any future issuance of additional authorized shares of our common stock could dilute future earnings per share, book value per share and voting power of existing stockholders. Depending upon the circumstances under which such shares are issued, such issuance may reduce stockholders equity per share and may reduce the percentage ownership of common stock of existing stockholders.

*Possible Anti-Takeover Effect from Future Issuances of Additional Shares.* Any future issuance of additional shares also may have an anti-takeover effect by making it more difficult to engage in a merger, tender offer, proxy contest or assumption of control of a large voting block of our common stock. Our board of directors could impede a takeover attempt by issuing additional shares and thereby diluting the voting power of other outstanding shares and increasing the cost of a takeover. A future issuance of additional shares of common stock could be made to render more difficult an attempt to obtain control of us, even if it appears to be desirable to a majority of stockholders, and it may be more difficult for our stockholders to obtain an acquisition premium for their shares or to remove incumbent management. Although the increase in the number of authorized shares of our common stock may have an anti-takeover effect, the amendment to our certificate of incorporation has been proposed for the reasons stated above under the heading "— Increase in Authorized Shares of our Common Stock," and our board of directors has no present intention to use the proposed increase in the authorized shares of our common stock as a measure aimed at discouraging takeover efforts.

#### INFORMATION CONCERNING THE INVUS DESIGNEES TO OUR BOARD OF DIRECTORS

Following the initial investment, our board of directors will have eleven members, consisting of three individuals designated by Invus. The current eight members of our board of directors will continue to serve as our directors. **You are not being asked to vote for the election of directors.**

#### Invus Designees

The following individuals are expected to be Invus' designees for election as members of our board of directors upon completion of the Invus transaction.

*Philippe J. Amouyal* 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. 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 is a director of Weight Watchers International, Inc., as well as a number of private companies in which Invus has invested.

*Raymond 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.

*Christopher J. Sobecki* is a managing director of The Invus Group, LLC, which he joined in 1989. Mr. Sobecki has served on the board of directors of numerous companies in which Invus has invested and is currently on the boards of directors of Weight Watchers International, Inc. and NitroMed, Inc., as well as a number of private companies in which Invus has invested. He holds a B.S. in industrial engineering from Purdue University and an M.B.A. from Harvard University.

#### Continuing Directors

The following individuals are current directors who will continue as members of our board of directors after the Invus transaction.

*Samuel L. Barker, Ph.D.* has been a director since March 2000 and became chairman of our board of directors in March 2005. 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 AtheroGenics, Inc. and Cadence Pharmaceuticals, Inc. Dr. Barker received his B.S. from Henderson State College, his M.S. from the University of Arkansas and his Ph.D. from Purdue University.

*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. He is a member of the National Academy of Sciences. Dr. Lefkowitz received his B.A. from Columbia University and his M.D. from Columbia University College of Physicians and Surgeons.

*Barry Mills, J.D., Ph.D.* has been a director since June 2006. Dr. Mills has been the president of Bowdoin College since 2001 and previously served as deputy presiding partner of Debevoise & Plimpton LLP, where he spent more than twenty years as an attorney focusing on corporate law, real estate and corporate finance. He currently serves as a director of Maine Bank & Trust Co., a Maine bank subsidiary of Chittenden Bank, and Galileo Fund Management Limited, as well as on several philanthropic boards. Dr. Mills received his A.B. from Bowdoin College, his Ph.D. from Syracuse University and his J.D. from the Columbia University School of Law.

*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.

*Frank P. Palantoni* has been a director since November 2004. 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.

*Clayton S. Rose, Ph.D.* has been a director since July 2004. Dr. Rose has been a senior lecturer at Harvard Business School since July 2007, and has also taught at Columbia University's Graduate School of Business and New York University's Stern School of Business. From 1981 through 2000, Dr. Rose worked at JP Morgan & Co, Inc. He held a series of senior management positions at JP Morgan, including heading each of the firm's Global Investment Banking and Global Equities divisions and serving as a member of the firm's executive committee. He also served as vice chairman and chief operating officer of the investment bank of JP Morgan Chase & Co. following the merger of the two firms. Dr. Rose serves as a director of Public/Private Ventures, is a member of the board of managers of Highbridge Capital, is a trustee of the National Opinion Research Center, and is a member of the Council for the Graduate School of Business at the University of Chicago. He received his A.B. and M.B.A. from the University of Chicago and his M.A. and Ph.D. from the University of Pennsylvania.

*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. Dr. Sands is a member of the board of directors of the Texas Institute for Genomic 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.

*Kathleen M. Wiltsey* has been a director since February 2007. From 1984 through 1998, Ms. Wiltsey served in a series of senior marketing and business development positions at Amgen Inc., including as co-product development team leader and marketing director for EPOGEN® and as vice president with responsibility for Amgen's product licensing function. From May to October 2006, Ms. Wiltsey served the X Prize Foundation as executive director for the development and launch of the Archon X PRIZE for Genomics, a global technology competition to dramatically reduce the cost of sequencing human genomes and accelerate personalized medicine. Ms. Wiltsey has served in a variety of business and corporate development advisory roles for numerous biotechnology companies and is currently vice president of the board of The Associates of the California Institute of Technology. She holds a B.S. from the Colorado School of Mines and an M.B.A. from Harvard University.

#### **STOCK OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT**

The following table presents information regarding the beneficial ownership of our common stock as of July 19, 2007 by:

- each of the individuals listed in "Executive Compensation — Summary Compensation Table" in our proxy statement for our 2007 annual meeting;
- 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 SEC computing the number of shares beneficially owned by a person and the percentage ownership of that person. Shares of common stock under options held by that person that are currently exercisable or exercisable within 60 days of July 19, 2007 are considered outstanding. These shares, however, are not considered outstanding when computing the percentage ownership of each other person.

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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 ownership prior to the initial investment is based on 85,965,249 shares of common stock outstanding on July 19, 2007. Percentage ownership after the initial investment takes into account the approximately 50.8 million shares to be issued to Invus in the initial investment and assumes that the only change in the ownership since July 19, 2007 is as a result of the consummation of the initial investment. 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					
	Before the Initial Investment			After the Initial Investment		
	Number of Shares Beneficially Owned	Shares Issuable Pursuant to Options or Warrants Exercisable Within 60 Days of July 19, 2007	Percentage Ownership Before Initial Investment	Number of Shares Beneficially Owned	Shares Issuable Pursuant to Options or Warrants Exercisable Within 60 Days of July 19, 2007	Percentage Ownership After Initial Investment
Invus Public Equities, L.P., Invus, L.P. and related parties(1)	3,891,108	16,498,353	19.9%	54,716,108	—	40.0%
Royce & Associates, LLC(2)	9,285,600	—	10.8%	9,285,600	—	6.8%
Robert C. McNair(3)	5,949,400	—	6.9%	5,949,400	—	4.4%
Barclays Global Investors, NA and Barclays Global Fund Advisors(4)	5,506,677	—	6.4%	5,506,677	—	4.0%
Symphony Capital Partners, L.P., Symphony Strategic Partners, LLC and related parties(5)	5,329,614	—	6.2%	5,329,614	—	3.9%
Arthur T. Sands, M.D., Ph.D.(6)	1,560,162	2,238,608	4.3%	1,560,162	2,238,608	2.7%
Julia P. Gregory(7)	55,047	808,675	1.0%	55,047	808,675	*
Alan J. Main, Ph.D.	—	519,791	*	—	519,791	*
Jeffrey L. Wade, J.D.	3,000	815,274	*	3,000	815,274	*
Brian P. Zambrowicz, Ph.D.	101,600	1,051,779	1.3%	101,600	1,051,779	*
Samuel L. Barker, Ph.D.	7,000	100,666	*	7,000	100,666	*
Robert J. Lefkowitz, M.D.	—	71,333	*	—	71,333	*
Barry Mills, J.D., Ph.D.	25,000	10,333	*	25,000	10,333	*
Alan S. Nies, M.D.	—	54,833	*	—	54,833	*
Frank P. Palantoni	—	30,333	*	—	30,333	*
Clayton S. Rose, Ph.D.	25,000	41,833	*	25,000	41,833	*
Kathleen M. Wiltsey	—	3,000	*	—	3,000	*
All directors and executive officers as a group(5)(6) (16 persons)	1,790,009	6,642,652	9.1%	1,790,009	6,642,652	5.9%

\* Represents beneficial ownership of less than 1 percent.

- (1) Based upon a Schedule 13D filed with the SEC on June 27, 2007, reflecting (a) the beneficial ownership of 3,891,108 shares of our common stock by Invus Public Equities, L.P., Invus Public Equities Advisors, LLC, Ulys, L.L.C. and Raymond Debbane, each of which may be deemed to have sole voting and investment power with respect to such shares, and (b) the beneficial ownership of a warrant to purchase 16,498,353 shares of our common stock by Invus, L.P., Invus Advisors, L.L.C., Ulys, L.L.C. and Mr. Debbane, each of which may be deemed to have sole voting and investment power with respect to such shares. The address for Invus Public Equities, L.P., Invus Public Equities Advisors, LLC, Invus, L.P., Invus Advisors, L.L.C. and Ulys, L.L.C. is 750 Lexington Avenue, 30th Floor, New York, New York 10022. The

- address for Mr. Debbane is c/o Ulys, L.L.C., 750 Lexington Avenue, 30th Floor, New York, New York 10022.
- (2) Based upon a Schedule 13G filed with the SEC on January 23, 2007, reflecting the beneficial ownership of our common stock by Royce & Associates, LLC. The address for Royce & Associates, LLC is 1414 Avenue of the Americas, New York, New York 10019.
  - (3) Based upon a Schedule 13D filed with the SEC on July 18, 2003, reflecting the beneficial ownership of our common stock by RCM Financial Services, L.P. (4,250,000 shares), Cogene Biotech Ventures, L.P. (1,679,400 shares) and Palmetto Partners, Ltd. (20,000 shares). Mr. McNair has sole voting and investment power with respect to all of such shares. The address for Mr. McNair is 4400 Post Oak Parkway, Suite 1400, Houston, Texas 77027.
  - (4) Based upon a Schedule 13G filed with the SEC on January 23, 2007, reflecting the beneficial ownership of our common stock by Barclays Global Investors, NA (3,651,367 shares) and Barclays Global Fund Advisors (1,855,310 shares). Barclays Global Investors, NA has sole voting power with respect to 3,349,935 shares and sole investment power with respect to 3,651,367 shares. Barclays Global Fund Advisors has sole voting and investment power with respect to 1,855,310 shares. The address for Barclays Global Investors, NA and Barclays Global Fund Advisors is 45 Fremont Street, San Francisco, California 94105.
  - (5) Based upon a Schedule 13G filed with the SEC on June 25, 2007, reflecting (a) the beneficial ownership of 4,954,745 shares of our common stock by Symphony Capital Partners, L.P., Symphony Capital GP, L.P., Symphony GP, LLC, Mark Kessel, Neil J. Sandler and Harri V. Taranto and (b) the beneficial ownership of 374,869 shares of our common stock by Symphony Strategic Partners, LLC, Mr. Kessel, Mr. Sandler and Mr. Taranto. Symphony Capital Partners, L.P., Symphony Capital GP, L.P. and Symphony GP, LLC may be deemed to have sole voting and investment power with respect to 4,954,745 shares. Symphony Strategic Partners, LLC may be deemed to have sole voting and investment power with respect to 374,869 shares. Mr. Kessel, Mr. Sandler and Mr. Taranto may be deemed to have shared voting and investment power with respect to 5,329,614 shares. The address for Symphony Capital Partners, L.P., Symphony Capital GP, L.P., Symphony GP, LLC, Symphony Strategic Partners, LLC, Mr. Kessel, Mr. Sandler and Mr. Taranto is 875 Third Avenue, 18th Floor, New York, New York 10022.
  - (6) 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.
  - (7) The number of shares beneficially owned by Ms. Gregory includes 4,847 shares held in the name of dependent children and trusts for their benefit of which she serves as a trustee.

#### **ABSENCE OF APPRAISAL RIGHTS**

We are incorporated in the State of Delaware and, accordingly, are subject to the Delaware General Corporation Law. Under the Delaware General Corporation Law, our stockholders are not entitled to appraisal rights with respect to either of the proposals to be acted upon at the special meeting.

#### **HOUSEHOLDING OF DISCLOSURE DOCUMENTS**

The SEC has approved a rule allowing us to send a single proxy statement to any household at which two or more stockholders reside if we believe the stockholders are members of the same family. This rule benefits both you and us by reducing the volume of duplicate information received at your household and helping to reduce our expenses. The rule applies to our annual reports, proxy statements and information statements. Each stockholder will continue to receive a separate proxy card or voting instruction card.

If your household received a single proxy statement, but you would prefer to receive your own copy, please contact our transfer agent, Mellon Investor Services L.L.C., by calling their toll-free number, (800) 635-9270. If you would like to receive your own set of our disclosure documents in future years, follow

the instructions described below. Similarly, if you share an address with another stockholder and together both of you would like to receive only a single set of our disclosure documents, follow these instructions:

- If your shares are registered in your own name, please contact our transfer agent, Mellon Investor Services, and inform them of your request by calling them at (800) 635-9270 or writing them at 480 Washington Boulevard, Jersey City, New Jersey 07310.
- If a broker or other nominee holds your shares, please contact ADP and inform them of your request by calling them at (888) 603-5847 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.

#### **STOCKHOLDER PROPOSALS FOR THE 2008 ANNUAL MEETING 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 23, 2007. Any such proposal must also comply with SEC 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 23, 2007. You may contact the corporate secretary at our principal executive offices for a copy of the relevant bylaw provisions for making stockholder proposals.

#### **WHERE YOU CAN FIND MORE INFORMATION**

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.

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any reports, statements or other information we file at the SEC's public reference room at 450 Fifth Street, N.W., Washington, D.C., 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from commercial document retrieval services and the web site maintained by the SEC at [www.sec.gov](http://www.sec.gov).

We filed a Current Report on Form 8-K on June 19, 2007 reporting the execution of the securities purchase agreement by us and Invus. A copy of the securities purchase agreement and related documents are filed as exhibits to the Form 8-K.

#### **FORWARD-LOOKING STATEMENTS**

This proxy statement contains statements that do not directly or exclusively relate to historical facts. Such statements are "forward-looking statements." You can typically identify forward-looking statements by the use of forward-looking words, such as "may," "will," "could," "project," "believe," "anticipate," "expect," "estimate," "potential," "plan," "forecast," and other similar words. Forward-looking statements in this proxy statement include statements regarding the following:

- completion of the Invus transaction;
- use of the proceeds from the Invus transaction; and
- the amendment to our certificate of incorporation.

The forward-looking statements in this proxy statement reflect our intentions, plans, expectations, assumptions and beliefs about future events and are subject to risks, uncertainties and other factors, many of which are outside our control. Important factors could cause actual results to differ materially from the expectations expressed or implied in the forward-looking statements contained herein. Except as required by

law, we undertake no obligation to update or revise our forward-looking statements, whether as a result of new information, future events or otherwise.

**CAUTIONARY STATEMENT CONCERNING REPRESENTATIONS AND WARRANTIES CONTAINED IN THE SECURITIES PURCHASE AGREEMENT AND RELATED AGREEMENTS**

You should not rely upon the representations and warranties contained in the securities purchase agreement or the related agreements or the descriptions of such representations and warranties in this proxy statement, as factual information about us or Invus. These representations and warranties were made only for purposes of the securities purchase agreement and the related agreements, were made solely to us or Invus, as applicable, as of the dates indicated therein and are subject to modification or qualification by other disclosures made by us. The representations and warranties are reproduced and summarized in this proxy statement solely to provide information regarding the terms of the securities purchase agreement and the related agreements and not to provide you with any other information regarding us or Invus. Information about us can be found elsewhere in this proxy statement and in other public filings we make with the SEC. Information about Invus can also be found elsewhere in this proxy statement.

**FORM OF  
SECOND CERTIFICATE OF AMENDMENT  
TO  
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 Section 242 of the DGCL:

FIRST: That at a meeting of the Board of Directors of the Corporation, resolutions were duly adopted setting forth a proposed amendment of the Corporation's Restated Certificate of Incorporation, as amended, declaring such amendment to be advisable and calling a meeting of the Corporation's stockholders for consideration thereof. The resolution setting forth the proposed amendment is as follows:

RESOLVED that, subject to the approval of the stockholders of the Corporation, the Corporation's restated certificate of incorporation, as amended, be further amended by changing Section 4.01(a) of Article IV thereof so that, as amended, such Section shall be and read as follows:

"(a) The total number of shares of stock that the Corporation shall have the authority to issue is 305,000,000 shares of capital stock, consisting of (i) 5,000,000 shares of preferred stock, par value \$0.01 per share (the "Preferred Stock"), and (ii) 300,000,000 shares of common stock, par value \$0.001 per share (the "Common Stock")."

SECOND: That thereafter, pursuant to a resolution of its Board of Directors, a special meeting of the Corporation's stockholders was duly called and held upon notice in accordance with the provisions of Section 222 of the DGCL, at which meeting the necessary number of shares as required by applicable law were voted in favor of such amendment.

THIRD: That such amendment was duly adopted in accordance with the provisions of Section 242 of the DGCL.

IN WITNESS WHEREOF, the Corporation has caused this Second Certificate of Amendment to be signed by Jeffrey L. Wade, its Executive Vice President and General Counsel, this        day of        , 2007.

LEXICON PHARMACEUTICALS, INC.

By: \_\_\_\_\_  
Jeffrey L. Wade  
*Executive Vice President and General Counsel*

[MORGAN STANLEY LETTERHEAD]

16 June 2007

Board of Directors  
Lexicon Pharmaceuticals, Inc.  
8800 Technology Forest Place  
The Woodlands, TX 77381-1160

Members of the Board:

We understand that Lexicon Pharmaceuticals, Inc. ("Lexicon" or the "Company") and Invus, L.P. ("Invus") propose to enter into a Securities Purchase Agreement, substantially in the form of the draft dated 15 June 2007 (the "Securities Purchase Agreement"), which provides, among other things, that the Company shall issue and seek to Invus, and Invus shall purchase (the "Initial Investment"): (a) a number of shares of Common Stock, that, when added to the shares of Company Common Stock already owned by Invus and its affiliates (including those issued upon exercise of any Warrants), equal 19.9% of the aggregate number of shares of common stock of the Company, par value \$0.001 per share (the "Company Common Stock") outstanding as of the Initial Investment Closing Date, for a per share price of \$3.0915, and (b) a number of shares of Company Common Stock that, when added to the number of shares of Company Common Stock already owned by Invus and its affiliates and the number of shares subject to clause (a) above, equal 40% of the aggregate number of shares of Company Common Stock outstanding as of the Initial Investment Closing Date, for a purchase price equal to \$4.50 per share. The terms and conditions of the transaction are more fully set forth in the Securities Purchase Agreement. Capitalized terms used but not otherwise defined herein have the meaning ascribed to them in the Securities Purchase Agreement.

You have asked for our opinion as to whether the consideration to be received by the Company in connection with the Initial Investment pursuant to the Securities Purchase Agreement is fair from a financial point to the Company.

For purposes of the opinion set forth herein, we have:

- i) reviewed certain publicly available financial statements and other business and financial information of the Company;
- ii) reviewed certain internal financial statements and other financial and operating data concerning the Company prepared by the management of the Company;
- iii) reviewed certain financial projections prepared by the management of the Company;
- iv) discussed the past and current operations and financial condition and the prospects of the Company with senior executives of the Company;
- v) reviewed the reported prices and trading activity for the Company Common Stock; vi) compared the prices and trading activity of the Company Common Stock with that of certain other comparable publicly-traded companies and their securities;
- vii) reviewed the financial terms, to the extent publicly available, of certain comparable acquisition transactions;
- viii) participated in discussions and negotiations among representatives of the Company and Invus, L.P.;
- ix) reviewed the Securities Purchase Agreement, the Registration Rights Agreement, the Warrant Agreement, and the Stockholders' Agreement; and



x) performed such other analyses reviewed such other information and considered such other factors as we have deemed appropriate.

We have assumed and relied upon without independent verification the accuracy and completeness of the information reviewed by us for the purposes of this opinion. With respect to the financial projections, we have assumed that they have been reasonably prepared on bases reflecting the best currently available estimates and judgments of the future financial performance of the Company. In addition, we have assumed that the Initial Investment will be consummated in accordance with the terms set forth in the Securities Purchase Agreement without any waiver, amendment or delay of any terms or conditions. We are not legal, tax or regulatory advisors. We are financial advisors only and have relied upon, without independent verification, the assessment of the Company and its legal, tax or regulatory advisors with respect to such matters. We have not made any independent valuation or appraisal of the assets or liabilities of the Company, nor have we been furnished with any such appraisals. Our opinion is necessarily based on economic, market and other conditions as in effect on, and the information made available to us as of, the date hereof).

In arriving at our opinion, we were not authorized to solicit, and did not solicit, interest from any party with respect to the acquisition of the Company or any of its assets, nor did we negotiate with any of the parties, other than Invus, which expressed interest to us in the possible acquisition of the Company or certain of its constituent businesses.

We have acted as financial advisor to the Board of Directors of the Company in connection with this transaction and will receive a fee for our services, a substantial portion of which is contingent upon the closing of the Initial Investment. In the past, Morgan Stanley & Co. Incorporated and its affiliates have provided and financing services for the Company and have received fees for the rendering of these services. Morgan Stanley may also seek to provide such services to Invus in the future and will receive fees for the rendering of these services. In the ordinary course of our trading, brokerage, investment management and financing activities, Morgan Stanley or its affiliates may at any time hold long or short positions, and may trade or otherwise effect transactions, for our own account or the accounts of customers, in debt or equity securities or senior loans of Invus, the Company or any other company or any currency or commodity that may be involved in this transaction.

It is understood that this letter is for the information of the Board of Directors of the Company and may not be used for any other purpose without our prior written consent, which shall not be unreasonably withheld. In addition, Morgan Stanley expresses no opinion or recommendation as to how the shareholders of the Company should vote at the shareholders' meeting to be held in connection with the Initial Investment.

Based on the foregoing, we are of the opinion on the date hereof that the consideration to be received by the Company in connection with the Initial Investment pursuant to the Securities Purchase Agreement is fair from a financial point of view to the Company.

Very truly yours,

MORGAN STANLEY & CO. INCORPORATED

By:     /s/ Jessica Chutter      
Jessica Chutter  
Managing Director

B-2

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**THE BOARD OF DIRECTORS RECOMMENDS A VOTE FOR PROPOSALS 1 AND 2.**

Please Mark Here for Address Change or Comments SEE REVERSE SIDE

**THIS PROXY WILL BE VOTED AS DIRECTED OR, IF NO DIRECTION IS INDICATED, WILL BE VOTED:**  
**"FOR"** the Invis transaction, which includes, among other things, the issuance by us of approximately 50.8 million shares of our common stock for approximately \$205 million and may include the issuance of additional shares of our common stock in up to two rights offerings pursuant to a securities purchase agreement by and among us and Invis, L.P., dated as of June 17, 2007, as it may be amended from time to time; and **"AGAINST"** the proposal to approve an amendment to our restated certificate of incorporation to increase the number of authorized shares of our common stock from 120 million to 300 million.

<p>1. Approval of the Invis transaction, which includes, among other things, the issuance by us of approximately 50.8 million shares of our common stock for approximately \$205 million and may include the issuance of additional shares of our common stock in up to two rights offerings pursuant to a securities purchase agreement by and among us and Invis, L.P., dated as of June 17, 2007, as it may be amended from time to time.</p>	<p>FOR <input type="checkbox"/></p> <p>AGAINST <input type="checkbox"/></p> <p>ABSTAIN <input type="checkbox"/></p>	<p>2. Approval of an amendment to the Company's restated certificate of incorporation increasing the number of authorized shares of our common stock from 120 million to 300 million.</p>	<p>FOR <input type="checkbox"/></p> <p>AGAINST <input type="checkbox"/></p> <p>ABSTAIN <input type="checkbox"/></p>
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If you plan to attend the meeting in person, please mark the following box.

Dated \_\_\_\_\_, 2007

\_\_\_\_\_  
(Signature)

\_\_\_\_\_  
(Signature if held jointly)

Please date, sign as name appears at the left, and return promptly. If the shares are registered in the names of two or more persons, each should sign. When signing as Corporate Officer, President, Executor, Administrator, Trustee or Guardian, please give full title. Please note any changes in your address alongside the address as it appears in the proxy.

**▲ FOLD AND DETACH HERE ▲**

**WE ENCOURAGE YOU TO TAKE ADVANTAGE OF INTERNET OR TELEPHONE VOTING, BOTH ARE AVAILABLE 24 HOURS A DAY, 7 DAYS A WEEK.**

**Internet and telephone voting is available through 11:59 PM Eastern Time the day prior to the special meeting day.**

Your internet or telephone vote authorizes the named proxies to vote your shares in the same manner as if you marked, signed and returned your proxy card.

<p style="text-align: center;"><b>INTERNET</b>  <a href="http://www.proxyvoting.com/lxrx">http://www.proxyvoting.com/lxrx</a>                  Use the internet to vote your proxy. Have your proxy card in hand when you access the web site.</p>	OR	<p style="text-align: center;"><b>TELEPHONE</b>  <b>1-866-540-5760</b>                  Use any touch-tone telephone to vote your proxy. Have your proxy card in hand when you call.</p>
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If you vote your proxy by Internet or by telephone, you do NOT need to mail back your proxy card. To vote by mail, mark, sign and date your proxy card and return it in the enclosed postage-paid envelope.

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**PROXY**  
**LEXICON PHARMACEUTICALS, INC.**  
**SPECIAL MEETING OF STOCKHOLDERS**  
**AUGUST 23, 2007**

**THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS OF**  
**LEXICON PHARMACEUTICALS, INC.**

The undersigned hereby appoints Arthur T. Sands and Jeffrey L. Wade, and each of them, as proxies and attorneys-in-fact, with the power to act without the other and with power of substitution, to represent the undersigned at the Special Meeting of Stockholders of Lexicon Pharmaceuticals, Inc. (the "Company") to be held at The Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas, on August 23, 2007, at 1:30 p.m., local time, and any adjournments or postponements thereof, and to vote all of the shares of stock the undersigned would be entitled to vote if personally present at such meeting (1) as provided on the other side of this proxy and (2) in their discretion, on such other business as may properly come before such meeting or any adjournment or postponement thereof.

(Continued and to be marked, dated and signed on other side)

Address Change/Comments (Mark the corresponding box on the reverse side)

▲ FOLD AND DETACH HERE ▲

**You can now access your LEXICON PHARMACEUTICALS, INC. account online.**

Access your Lexicon Pharmaceuticals, Inc. stockholder account online via Investor ServiceDirect® (ISD).

Mellon Investor Services LLC, Transfer Agent for Lexicon Pharmaceuticals, Inc., now makes it easy and convenient to get current information on your shareholder account.

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**PRINT AUTHORIZATION** (THIS BOXED AREA DOES NOT PRINT)

To commence printing on this proxy card please sign, date and fax this card to: 212-691-9013

SIGNATURE: \_\_\_\_\_ DATE: \_\_\_\_\_ TIME: \_\_\_\_\_

Mark this box if you would like the Proxy Card EDGARized:  ASCII  EDGAR II (HTML)  
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