

OMB APPROVAL

OMB Number: 3235-0059
Expires: January 31, 2008
Estimated average burden
hours per response.....14

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.)

Filed by the Registrant [X]
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))
- [X] Definitive Proxy Statement
- [] Definitive Additional Materials
- [] Soliciting Material Pursuant to Section 240.14a-12

LEXICON GENETICS INCORPORATED

(Name of Registrant as Specified In Its Charter)

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

Payment of Filing Fee (check the appropriate box):

- [X] No fee required.
- [] Fee computed on table below per Exchange Act Rules 14a-6(i)(4) and 0-11.

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

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:

PERSONS WHO POTENTIALLY ARE TO RESPOND TO THE COLLECTION OF INFORMATION
CONTAINED IN THIS FORM ARE NOT REQUIRED TO RESPOND UNLESS THE FORM DISPLAYS A
CURRENTLY VALID OMB CONTROL NUMBER.

(LEXICON LOGO)

March 24, 2006

TO OUR STOCKHOLDERS:

I am pleased to invite you to attend the 2006 annual meeting of stockholders of Lexicon Genetics Incorporated to be held on Wednesday, April 26, 2006 at 1:30 p.m., local time, at The Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas. We have enclosed with this letter:

- an official notice of the annual meeting;
- a proxy statement that describes the matters to be considered and acted upon at the annual meeting; and
- a form of proxy that we are asking you to complete and return to us, indicating your vote with respect to the matters described in the proxy statement.

Your vote is important, regardless of the number of shares that you hold. Whether or not you plan to attend the annual meeting, I hope you will vote as soon as possible by signing and returning the enclosed form of proxy in the postage-paid envelope we have provided for that purpose.

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

Sincerely,

/s/ Arthur T. Sands

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

LEXICON GENETICS INCORPORATED
8800 TECHNOLOGY FOREST PLACE
THE WOODLANDS, TEXAS 77381
(281) 863-3000

NOTICE OF ANNUAL MEETING OF STOCKHOLDERS
TO BE HELD APRIL 26, 2006

TO OUR STOCKHOLDERS:

The annual meeting of stockholders of Lexicon Genetics Incorporated will be held on Wednesday, April 26, 2006 at 1:30 p.m., local time, at The Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas, to:

- elect two Class III directors;
- ratify and approve the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2006; and
- act on any other business that properly comes before the annual meeting.

You are entitled to vote at the annual meeting only if you are the record owner of shares of our common stock at the close of business on March 7, 2006.

It is important that your shares be represented at the annual 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. If you are present at the annual meeting, and wish to do so, you may revoke the proxy and vote in person.

By order of the board of directors,

/s/ Jeffrey L. Wade

Jeffrey L. Wade
Secretary

The Woodlands, Texas
March 24, 2006

LEXICON GENETICS INCORPORATED
8800 TECHNOLOGY FOREST PLACE
THE WOODLANDS, TEXAS 77381
(281) 863-3000

PROXY STATEMENT
FOR
ANNUAL MEETING OF STOCKHOLDERS
TO BE HELD APRIL 26, 2006

GENERAL INFORMATION

PURPOSE OF THIS PROXY STATEMENT

We have prepared this proxy statement to solicit proxies on behalf of our board of directors for use at our 2006 annual meeting of stockholders and any adjournment or postponement of such meeting. We are mailing this proxy statement and the accompanying notice of annual meeting of stockholders and form of proxy to our stockholders on or about March 24, 2006.

TIME AND PLACE OF ANNUAL MEETING

The annual meeting will be held on Wednesday, April 26, 2006 at 1:30 p.m., local time, at The Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas.

MATTERS TO BE CONSIDERED AT THE ANNUAL MEETING

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

- the election of two Class III directors;
- a proposal to ratify and approve the appointment of Ernst & Young LLP as our independent auditors for the fiscal year ending December 31, 2006.

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

RECORD DATE FOR DETERMINING ENTITLEMENT TO VOTE

You are entitled to vote at the annual meeting if you were the record owner of shares of our common stock as of the close of business on March 7, 2006, the record date for the annual meeting established by our board of directors.

HOW TO VOTE YOUR SHARES

You may vote in person at the annual meeting or by proxy. To ensure that your shares are represented at the annual meeting, we recommend you vote by proxy even if you plan to attend the annual meeting in person. Even if you vote by proxy, if you wish, you can revoke your proxy and vote in person at the annual meeting. If you want to vote at the annual meeting but your shares are held by an intermediary, such as a broker or bank, you will need to obtain from the intermediary either proof of your ownership of such shares as of March 7, 2006 or a proxy from such intermediary authorizing you to vote your shares at the meeting.

You may receive more than one proxy depending on how you hold your shares. If you hold your shares through 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 annual meeting.

QUORUM

We must have a quorum to conduct any business at the annual meeting. This means that at least a majority of our outstanding shares eligible to vote at the annual meeting must be represented at the annual meeting, either in person or by proxy. Abstentions are counted for purposes of determining whether a quorum is present. In addition, shares of our common stock held by intermediaries that are voted for at least one matter at the annual meeting will be counted as being present for purposes of determining a quorum for all matters, 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 64,565,161 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 annual meeting.

VOTE NEEDED TO APPROVE PROPOSALS

Our Class III directors will be elected by a plurality vote. As a result, if a quorum is present at the annual meeting, the two persons receiving the greatest number of votes will be elected to serve as our Class III directors. Withholding authority to vote for a director nominee will not affect the outcome of the election of directors.

The ratification and approval of the appointment of Ernst & Young LLP as our independent auditors for the year ending December 31, 2006 will require a majority of the votes cast with respect to such matter. Any other business that may properly come before the annual meeting for a vote will require a majority of the votes cast with respect to such matter unless a greater vote is required by law or our charter or bylaws. On any such matter, an abstention from voting will have the same effect as a vote against the proposal. Broker non-votes do not count as votes for or against these proposals and are not considered in calculating the number of votes necessary for approval.

HOW YOUR PROXY WILL BE VOTED

Giving us your proxy means that you are authorizing us to vote your shares at the annual meeting in the manner you direct. You may vote for our nominees for election as Class III directors or withhold your vote for any one or more of those nominees. You may vote for or against the appointment of Ernst & Young LLP as our independent auditors for the year ending December 31, 2006 or abstain from voting on that proposal.

If you sign and return the enclosed proxy card and do not withhold authority to vote for the election of our nominees for election as Class III directors, all of your shares will be voted for the election of those nominees. If you withhold authority to vote for one or more of our nominees for election as Class III directors, none of your shares will be voted for those nominees.

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

If you sign and return the enclosed proxy but do not specify how you want your shares voted, your shares will be voted in favor of our nominees for election as Class III directors and in favor of the appointment of Ernst & Young LLP as our independent auditors for the year ending December 31, 2006.

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

HOW TO REVOKE YOUR PROXY

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

Lexicon Genetics Incorporated
8800 Technology Forest Place
The Woodlands, Texas 77381
Attention: Corporate Secretary

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

INSPECTOR OF ELECTION

Mellon Investor Services L.L.C., our transfer agent and registrar, will count votes and provide a representative who will serve as an inspector of election for the annual meeting.

LIST OF STOCKHOLDERS ENTITLED TO VOTE

A list of our stockholders entitled to vote at the annual meeting will be available for inspection at the annual meeting. The stockholder list will also be available for inspection for ten days prior to the annual meeting at our corporate offices located at 8800 Technology Forest Place, The Woodlands, Texas. Any inspection of this list at our offices will need to be conducted during ordinary business hours. If you wish to conduct an inspection of the stockholder list, we request that you please contact our corporate secretary before coming to our offices.

SOLICITATION OF PROXIES AND EXPENSES

We are asking for your proxy on behalf of our board of directors. We will bear the entire cost of preparing, printing and soliciting proxies. We will send 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. Our directors, officers and employees may solicit proxies by mail, in person or by telephone or other electronic communication. Our directors, officers and employees will not receive additional compensation for their solicitation efforts, but they will be reimbursed for any out-of-pocket expenses they incur.

HOUSEHOLDING OF ANNUAL DISCLOSURE DOCUMENTS

The Securities and Exchange Commission has approved a rule allowing us to send a single set of our annual report and 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 set of disclosure documents for this year, 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 annual 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 annual 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.

STOCK OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

The following table presents information regarding the beneficial ownership of our common stock as of March 7, 2006 by:

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

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission computing the number of shares beneficially owned by a person and the percentage ownership of that person. Shares of common stock under options held by that person that are currently exercisable or exercisable within 60 days of March 7, 2006 are considered outstanding. These shares, however, are not considered outstanding when computing the percentage ownership of each other person.

Except as indicated in the footnotes to this table and pursuant to state community property laws, each stockholder named in the table has sole voting and investment power for the shares shown as beneficially owned by them. Percentage of ownership is based on 64,565,161 shares of common stock outstanding on March 7, 2006. Unless otherwise indicated in the footnotes, the address of each of the individuals named below is: c/o Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas 77381.

| BENEFICIAL OWNERSHIP | | | |
|---|---|--|-------------------------|
| | NUMBER OF SHARES BENEFICIALLY OWNED | SHARES ISSUABLE PURSUANT TO OPTIONS EXERCISABLE WITHIN 60 DAYS OF MARCH 7, 2006 | PERCENTAGE OWNERSHIP |
| Royce & Associates, LLC (1) | 8,067,100 | -- | 12.5% |
| Robert C. McNair (2) | 5,949,400 | -- | 9.2% |
| Barclays Global Investors, NA and Barclays Global Fund Advisors (3) | 4,918,155 | -- | 7.6% |
| Baylor College of Medicine (4) | 4,036,060 | -- | 6.3% |
| Invus Public Equities, L.P. and related parties (5) | 3,300,600 | -- | 5.1% |
| Arthur T. Sands, M.D., Ph.D. (6) | 1,465,162 | 2,256,914 | 5.6% |
| Julia P. Gregory (7) | 55,047 | 702,520 | 1.2% |
| Jeffrey L. Wade, J.D. | 3,000 | 715,264 | 1.1% |
| Brian P. Zambrowicz, Ph.D. | 63,900 | 1,013,225 | 1.6% |
| Alan J. Main, Ph.D. | -- | 448,432 | * |
| Samuel L. Barker, Ph.D. | 7,000 | 74,000 | * |
| C. Thomas Caskey, M.D (8) | 6,500 | 224,000 | * |
| Patricia M. Cloherty | -- | 64,000 | * |
| Robert J. Lefkowitz, M.D. | -- | 58,000 | * |
| Alan S. Nies, M.D. | -- | 32,375 | * |
| Frank P. Palantoni | -- | 9,000 | * |
| Clayton S. Rose | 10,000 | 20,500 | * |
| All directors and executive officers as a group (6)(7)(8) (15 persons) | 1,617,909 | 6,501,463 | 11.4% |

* Represents beneficial ownership of less than 1 percent.

(1) Based upon a Schedule 13G filed with the SEC on January 30, 2006, 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.

- (2) 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.
- (3) Based upon a Schedule 13G filed with the SEC on January 26, 2006, reflecting the beneficial ownership of our common stock by Barclays Global Investors, NA (3,600,418 shares) and Barclays Global Fund Advisors (1,317,737 shares). Barclays Global Investors, NA has sole voting power with respect to 3,157,161 shares and sole investment power with respect to 3,600,418 shares. Barclays Global Fund Advisors has sole voting and investment power with respect to 1,317,737 shares. The address for Barclays Global Investors, NA and Barclays Global Fund Advisors is 45 Fremont Street, San Francisco, California 94105.
- (4) Based upon a Schedule 13G/A filed with the SEC on January 5, 2006, reflecting the beneficial ownership of our common stock by Baylor College of Medicine and BCM Technologies, Inc., a wholly owned subsidiary of Baylor College of Medicine. The number of shares beneficially owned includes 28,940 shares owned by BCM Technologies, Inc. The address of Baylor College of Medicine is One Baylor Plaza, T-100 MS BCM 203, Houston, Texas 77030-3498.
- (5) Based upon a Schedule 13G filed with the SEC on March 9, 2006 reflecting the beneficial ownership of our common stock by Invus Public Equities, L.P., Invus Public Equities Advisors, L.L.C., Ulys, L.L.C. and Raymond Debbane, each of which have shared voting and investment power with respect to such shares. The address for Invus Public Equities, L.P., Invus Public Equities Advisors, L.L.C., Ulys, L.L.C. and Mr. Debbane is 135 East 57th Street, 30th 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.
- (8) The number of shares beneficially owned by Dr. Caskey includes 200 shares held for the benefit of minor children.

SECTION 16(A) BENEFICIAL OWNERSHIP REPORTING COMPLIANCE

Section 16(a) of the Exchange Act requires our directors and executive officers, and persons who own more than 10% of our common stock, to file initial reports of ownership and reports of changes in ownership of our common stock with the Securities and Exchange Commission. Directors, executive officers and greater than 10% stockholders are required by Securities and Exchange Commission regulations to furnish us with copies of all such forms that they file.

To our knowledge, based solely on our review of the copies of such reports received by us and on written representations by certain reporting persons that no reports on Form 5 were required, we believe that during the fiscal year ended December 31, 2005, all Section 16(a) filing requirements applicable to our executive officers, directors and 10% stockholders were complied with in a timely manner.

EQUITY COMPENSATION PLAN INFORMATION

The following table presents aggregate summary information as of December 31, 2005 regarding the common stock that may be issued upon exercise of options, warrants and rights under all of our existing equity compensation plans, including our 2000 Equity Incentive Plan, 2000 Non-Employee Directors' Stock Option Plan and Coelacanth Corporation 1999 Stock Option Plan.

| PLAN CATEGORY | (A) NUMBER OF SECURITIES TO BE ISSUED UPON EXERCISE OF OUTSTANDING OPTIONS, WARRANTS AND RIGHTS | (B) WEIGHTED AVERAGE EXERCISE PRICE PER SHARE OF OUTSTANDING OPTIONS, WARRANTS AND RIGHTS | (C) NUMBER OF SECURITIES REMAINING AVAILABLE FOR FUTURE ISSUANCE UNDER EQUITY COMPENSATION PLANS (EXCLUDING SECURITIES REFLECTED IN COLUMN (A)) |
|---|---|---|---|
| Equity compensation plans approved by security holders(1)..... | 13,728,330 | \$6.3793 | 1,353,866(3)(4)(5) |
| Equity compensation plans not approved by security holders(2)... | 74,051 | 2.3203 | -- |
| Total..... | 13,802,381 | \$6.3575 | 1,353,866 |

- (1) Consists of shares of our common stock issued or remaining available for issuance under our 2000 Equity Incentive Plan and 2000 Non-Employee Directors' Stock Option Plan.

(2) Consists of shares of our common stock issuable upon the exercise of options granted under the Coelacanth Corporation 1999 Stock Option Plan, which we assumed in connection with our July 2001 acquisition of Coelacanth Corporation, but does not include warrants to purchase 16,483 shares of common stock at a weighted average exercise price of \$11.93 per share, which we also assumed in connection with our acquisition of Coelacanth.

- (3) Includes 1,011,866 shares available for future issuance under our 2000 Equity Incentive Plan, some or all of which may be awarded as stock bonuses.
- (4) Our 2000 Equity Incentive Plan provides that on each January 1, the number of shares available for issuance under the plan will be automatically increased by the greater of (i) five percent of our outstanding shares on a fully-diluted basis or (ii) the number of shares that could be issued under awards granted under the plan during the prior year. Our board of directors may provide for a lesser increase in the number of shares available for issuance under the plan.
- (5) Our 2000 Non-Employee Directors' Stock Option Plan provides that on the day following each annual meeting of stockholders, the number of shares available for issuance under the plan will be automatically increased by the greater of (i) 0.3% of our outstanding shares on a fully-diluted basis or (ii) the number of shares that could be issued under options granted under the plan during the prior year. Our board of directors may provide for a lesser increase in the number of shares available for issuance under the plan.

PROPOSAL NUMBER 1:
ELECTION OF DIRECTORS

Our board of directors, which currently has eight members, is divided or "classified" into three classes. Directors in each class are elected to hold office for a term ending on the date of the third annual meeting following the annual meeting at which they were elected. The current term of our Class III directors will expire at this annual meeting. The current terms of our Class I and Class II directors will expire at our 2007 and 2008 annual meetings of stockholders, respectively.

The board of directors has nominated and urges you to vote for the election of the individuals identified below, who have been nominated to serve as Class III directors until our 2009 annual meeting of stockholders or until their successors are duly elected and qualified. Each of these individuals is a member of our present board of directors. Your signed proxy will be voted for the nominees named below unless you specifically indicate on the proxy that you are withholding your vote.

It is our policy to encourage the members of our board of directors to attend all annual meetings of stockholders. Five members of our board of directors attended our 2005 annual meeting of stockholders.

NOMINEES FOR CLASS III DIRECTORS

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

| NAME | AGE | POSITION WITH THE COMPANY | YEAR FIRST BECAME A DIRECTOR |
|------------------------------|-----|---------------------------|------------------------------|
| Arthur T. Sands, M.D., Ph.D. | 44 | Director (Class III) | 1995 |
| Frank P. Palantoni | 48 | Director (Class III) | 2004 |

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

Frank P. Palantoni has been a director since November 2004. Mr. Palantoni has served as president and chief operating officer of Prestige Brands Holding, Inc. since August 2005 and as a director since January 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.

THE BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE "FOR" THE FOREGOING NOMINEES FOR ELECTION AS CLASS III DIRECTORS.

CURRENT AND CONTINUING DIRECTORS

The current directors of the Company are identified below. Dr. Caskey's term as a director will expire at this annual meeting, and he is not standing for re-election.

| NAME | AGE | POSITION WITH THE COMPANY |
|--------------------------------|-----|--|
| Arthur T. Sands, M.D., Ph.D. | 44 | President and Chief Executive Officer and Director (Class III) |
| Samuel L. Barker, Ph.D. (1)(2) | 63 | Chairman of the Board of Directors (Class II) |
| C. Thomas Caskey, M.D. | 67 | Director (Class III) |
| Patricia M. Cloherty (1) | 63 | Director (Class II) |
| Robert J. Lefkowitz, M.D. (3) | 62 | Director (Class I) |
| Alan S. Nies, M.D. | 68 | Director (Class I) |
| Frank P. Palantoni (2)(3) | 48 | Director (Class III) |
| Clayton S. Rose (1)(2) | 47 | Director (Class I) |

- (1) Member of the Audit Committee
- (2) Member of the Compensation Committee
- (3) Member of the Corporate Governance Committee

Information regarding the business experience of Dr. Sands and Mr. Palantoni is set forth above under the heading "--Nominees for Class III Directors."

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 received his B.S. from Henderson State College, his M.S. from the University of Arkansas and his Ph.D. from Purdue University.

C. Thomas Caskey, M.D. has been a director since April 2000 and was the chairman of our board of directors from April 2000 to March 2005. In January 2006, Dr. Caskey was appointed director and chief executive officer-elect of the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases, part of the University of Texas Health Science Center at Houston. Dr. Caskey was managing director of Cogene Biotech Ventures, Ltd., a venture capital firm, from March to October 2005 and served as president and chief executive officer of the firm from April 2000 to March 2005. He served as senior vice president, research at Merck Research Laboratories, a division of Merck & Co., Inc., from 1995 to March 2000 and as president of the Merck Genome Research Institute from 1996 to March 2000. Before joining Merck, Dr. Caskey served 25 years at Baylor College of Medicine in a series of senior positions, including chairman, Department of Human and Molecular Genetics and director, Human Genome Center. He is a member of the National Academy of Sciences. Dr. Caskey serves as a director of Luminex Corporation and several private companies. He received his B.A. from the University of South Carolina and his M.D. from Duke University Medical School

Patricia M. Cloherty has been a director since May 1998. Ms. Cloherty serves as chairman and chief executive officer of Delta Private Equity Partners, LLC, manager of the U.S. Russia Investment Fund and Delta Russia Fund, L.P., two venture capital funds formed to invest in Russian companies. She was appointed to the board of the U.S. Russia Investment Fund in 1995 by President Clinton, became chairman in 1998 and was elected chief executive officer of the fund in July 2003. From 1973 through 1999, she was general partner of Patricof & Co. Ventures, Inc., an international venture capital company, and successively served as senior vice president, president and co-chairman of that company. Ms. Cloherty served as deputy administrator of the United States Small Business Administration from 1977 to 1978. She is past president and chairman of the National Venture Capital Association. Ms. Cloherty serves as a director of several private companies and philanthropies. She holds a B.A. from the San Francisco College for Women and an M.A. and an M.I.A. from Columbia 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.

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.

Clayton S. Rose has been a director since July 2004. Mr. Rose has been an adjunct professor at Columbia University's Graduate School of Business since 2002, and has also taught at New York University's Stern School of Business. From 1981 through 2000, Mr. 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. Mr. Rose serves as a director of Mercantile Bankshares Corporation, Public/Private Ventures and The Reinvestment Fund 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 holds an M.A. from the University of Pennsylvania.

INDEPENDENCE OF THE BOARD OF DIRECTORS

After reviewing all relevant transactions and relationships between each member of the board of directors (and his or her family) and us, our senior management and our independent auditors, the board of directors has affirmatively determined that Samuel L. Barker, Ph.D., Patricia M. Cloherty, Robert J. Lefkowitz, M.D., Frank P. Palantoni and Clayton S. Rose, which members constitute a majority of the board of directors, are "independent" in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc.

BOARD COMMITTEES

Audit Committee. Our audit committee monitors the integrity of our financial statements, reviews our internal accounting procedures and oversees the qualifications, independence and performance of our independent auditors. The audit committee operates pursuant to a charter that was last amended and restated by the board of directors on October 26, 2005, a copy of which is attached to this proxy statement as Appendix A and appears on our website at www.lexicon-genetics.com under the caption "Investor Relations - Corporate Governance."

The current members of our audit committee are Clayton S. Rose (chair), Samuel L. Barker, Ph.D. and Patricia M. Cloherty. The board of directors, in its business judgment, has determined that Mr. Rose, Dr. Barker and Ms. Cloherty are "independent" in accordance with the provisions of the Securities Exchange Act of 1934, including all rules and regulations promulgated thereunder. The board of directors has further determined that Mr. Rose, Dr. Barker and Ms. Cloherty are "independent" in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc. The board of directors, in its business judgment, has also determined that Mr. Rose and Ms. Cloherty are "audit committee financial experts" as defined in Item 401(h) of Regulation S-K.

Compensation Committee. Our compensation committee evaluates the performance of management, determines the compensation of our executive officers and reviews general policy relating to compensation and benefits of our employees. The compensation committee also administers the issuance of stock options and other awards under our 2000 Equity Incentive Plan. The compensation committee operates pursuant to a charter that was approved by the board of directors on February 11, 2004, a copy of which appears on our website at www.lexicon-genetics.com under the caption "Investor Relations - Corporate Governance."

The current members of the compensation committee are Clayton S. Rose (chair), Samuel L. Barker, Ph.D. and Frank P. Palantoni. The board of directors, in its business judgment, has determined that Mr. Rose, Dr. Barker and Mr. Palantoni are "independent" in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc.

Corporate Governance Committee. Our corporate governance committee identifies individuals qualified to become members of our board of directors, selects candidates or nominees for director positions to be filled by the board of directors or our stockholders and develops appropriate corporate governance principles. The corporate governance committee operates pursuant to a charter that was approved by the board of directors on February 11, 2004, a copy of which appears on our website at www.lexicon-genetics.com under the caption "Investor Relations - Corporate Governance."

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

Any stockholder wishing to propose a potential director candidate may submit a recommendation in writing within the time frame specified in our bylaws. All such communications should be sent to 8800 Technology Forest Place, The Woodlands, Texas 77381, Attn: Corporate Governance Committee. Submissions should include the full name of the proposed candidate and a detailed description of the candidate's qualifications, business experience and other relevant biographical information.

The current members of the corporate governance committee are Frank P. Palantoni (chair) and Robert J. Lefkowitz, M.D. The board of directors, in its business judgment, has determined that Mr. Palantoni and Dr. Lefkowitz are "independent" in accordance with the applicable listing standards of The Nasdaq Stock Market, Inc.

BOARD AND COMMITTEE MEETINGS IN 2005

The board of directors met eight times, the audit committee met four times and the corporate governance committee met once in 2005. The compensation committee met six times in 2005 and took certain additional actions by unanimous written consent. During 2005, none of our directors attended fewer than 75 percent of the aggregate number of meetings of the board of directors and committees during the period served.

NON-EMPLOYEE DIRECTOR COMPENSATION

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

- an annual retainer of \$15,000 for service on the board of directors (\$30,000 for service as non-executive chairman of the board of directors), prorated for any partial year of service;
- an annual retainer of \$2,500 for service on each committee of the board of directors of which he or she is a member (\$5,000 for service as chairman of any such committee), prorated for any partial year of service;
- a fee of \$2,500 for each meeting of the board of directors that he or she attends in person (\$500 for each telephonic meeting of the board of directors in which he or she participates); and
- a fee of \$1,000 for each committee meeting that he or she attends in person other than in connection with a meeting of the full board of directors (\$500 for each telephonic committee meeting in which he or she participates).

Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, does not receive additional compensation for his service as a director. All directors are reimbursed for expenses in connection with attendance at board of directors and committee meetings.

Our 2000 Non-Employee Directors' Stock Option Plan provides for the grant of options to purchase shares of common stock to our non-employee directors. Non-employee directors first elected after the closing of our initial public offering in April 2000 receive an initial option to purchase 30,000 shares of common stock. In addition, all non-employee directors who have served in such capacity for six months receive an annual option to purchase 10,000 shares of common stock. All options granted under the non-employee directors' plan have an exercise price equal to the fair market value of our common stock on the date of grant.

The chairman of our board of directors receives an additional annual option under our 2000 Equity Incentive Plan to purchase 10,000 shares of common stock. All such options have an exercise price equal to the fair market value of our common stock on the date of grant.

The following table presents summary information for the year ended December 31, 2005 regarding the compensation of the non-employee members of our board of directors:

| NAME | ANNUAL RETAINER FEES | MEETING FEES | NUMBER OF SECURITIES UNDERLYING OPTIONS GRANTED (1) | ALL OTHER COMPENSATION |
|--------------------------------|-------------------------|--------------|---|---------------------------|
| Samuel L. Barker, Ph.D. | \$23,002 | \$14,000 | 10,000 | -- |
| C. Thomas Caskey, M.D. | \$11,808 | \$10,000 | 10,000 | \$88,334(2) |
| Patricia M. Cloherty. | \$22,500 | \$11,500 | 10,000 | -- |
| Robert J. Lefkowitz, M.D. | \$17,500 | \$ 9,500 | 10,000 | \$50,000(3) |
| Alan S. Nies, M.D. | \$15,000 | \$12,000 | 10,000 | \$75,000(4) |
| Frank P. Palantoni | \$20,904 | \$12,500 | -- | -- |
| Clayton S. Rose | \$21,425 | \$13,000 | 10,000 | -- |

(1) Consists of stock options granted at the time of our annual meeting of stockholders in April 2005 under the 2000 Non-Employee Directors' Stock Option Plan at an exercise price of \$4.40 per share, the fair market value of our common stock on the date of grant as determined in accordance with the plan.

(2) Consists of amounts payable to Dr. Caskey for his service as non-executive chairman of the board of directors through March 2005 and for his consulting services thereafter.

(3) Consists of amounts payable to Dr. Lefkowitz for his consulting services.

(4) Consists of amounts payable to Dr. Nies for his consulting services as chairman of our Medical Advisory Board.

CERTAIN TRANSACTIONS WITH DIRECTORS

We are party to a consulting agreement with C. Thomas Caskey, M.D. dated March 28, 2005, under which Dr. Caskey serves as a consultant to us on governmental affairs and other matters. Dr. Caskey receives payment of \$75,000 per year for his consulting services under the agreement. The agreement expires on March 28, 2006.

We are party to a consulting agreement with Robert J. Lefkowitz, M.D. dated March 31, 2003, under which Dr. Lefkowitz serves as a consultant to us on matters relating to our drug discovery and development efforts. Dr. Lefkowitz receives payment of \$50,000 per year for his consulting services under the agreement. The agreement has an initial term of one year and is automatically extended for additional one-year terms unless otherwise terminated by the parties.

We are party to a consulting agreement with Alan S. Nies, M.D. dated February 19, 2003, as amended, under which Dr. Nies serves as chairman of our Medical Advisory Board and provides consulting services on matters relating to our drug discovery and development efforts. Dr. Nies receives payment of \$75,000 per year for his consulting services under the agreement and received an option under our 2000 Equity Incentive Plan to purchase 2,500 shares of common stock at an exercise price of \$4.06 per share, the fair market value of our common stock on the date of grant as determined in accordance with the plan. The agreement has an initial term of one year and is automatically extended for additional one-year terms unless otherwise terminated by the parties.

CORPORATE GOVERNANCE GUIDELINES

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

STOCKHOLDER COMMUNICATIONS WITH THE BOARD OF DIRECTORS

We believe that our stockholders are currently provided a reasonable means to communicate with our board of directors and individual directors. As a result, our board of directors has not established a formal process for stockholders to send communications to the board of directors or individual directors. However, the corporate governance committee will consider, from time to time, whether adoption of a formal process for such stockholder communications has become necessary or appropriate. Stockholders may send communications to the board of directors or individual directors by mail at 8800 Technology Forest Place, The Woodlands, Texas 77381, Attn: Board of Directors.

CODE OF BUSINESS CONDUCT AND ETHICS

We have adopted a code of business conduct and ethics that applies to all of our directors, officers and employees, the text of which appears on our website at www.lexicon-genetics.com under the caption "Investor Relations - Corporate Governance." We intend to disclose on our website the nature of any amendment to or waiver from our code of business conduct and ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions within five business days following the date of such amendment or waiver. In the case of any such waiver, including an implicit waiver, we also intend to disclose the name of the person to whom the waiver was granted and the date of the waiver.

COMPENSATION COMMITTEE INTERLOCKS AND INSIDER PARTICIPATION

During 2005, Samuel L. Barker, Ph.D., Patricia M. Cloherty, Frank P. Palantoni and Clayton S. Rose served as members of the compensation committee of our board of directors. No member of the compensation committee serves as a member of the board of directors or compensation committee of any other entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

PROPOSAL NUMBER 2:
RATIFICATION AND APPROVAL OF INDEPENDENT AUDITORS

The board of directors has appointed the firm of Ernst & Young LLP as our independent auditors to make an examination of our accounts for the fiscal year ending December 31, 2006, subject to ratification by our stockholders. Representatives of Ernst & Young LLP, are expected to be present at the annual meeting, will have an opportunity to make a statement if they desire to do so and are expected to be available to respond to appropriate questions.

THE BOARD OF DIRECTORS RECOMMENDS THAT STOCKHOLDERS VOTE "FOR" RATIFICATION AND APPROVAL OF THE APPOINTMENT OF ERNST & YOUNG LLP AS OUR INDEPENDENT AUDITORS FOR THE FISCAL YEAR ENDING DECEMBER 31, 2006.

COMPENSATION OF INDEPENDENT AUDITORS

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

| | YEARS ENDED DECEMBER 31, | |
|-----------------------------|--------------------------|-----------|
| | 2005 | 2004 |
| | ----- | ----- |
| Audit fees(1)..... | \$260,500 | \$300,322 |
| Audit-related fees(2) | 19,000 | 45,326 |
| Tax fees(3)..... | 30,900 | 30,660 |
| All other fees(4)..... | -- | 375 |
| | ----- | ----- |
| | \$310,400 | \$376,683 |
| | ===== | ===== |

(1) "Audit fees" include professional services rendered for (i) the audit of our management's assessment of effective internal control over financial reporting, as required by the Sarbanes-Oxley Act of 2002, for the fiscal years ended December 31, 2004 and 2005, (ii) the audit of our annual financial statements for the fiscal years ended December 31, 2004 and 2005, (iii) the reviews of the financial statements included in our quarterly reports on Form 10-Q for such years and (iv) the issuance of consents and other matters relating to registration statements filed by us.

(2) "Audit-related fees" include assurance or related services reasonably related to our audit for the fiscal years ended December 31, 2004 and 2005. These fees related to the audit of the financial statements of our 401(k) plan and consultation concerning financial accounting and reporting standards.

(3) "Tax fees" include professional services related to the preparation of our tax returns, tax planning and other tax advice for the fiscal years ended December 31, 2004 and 2005.

(4) "All other fees" include products and services other than those disclosed as audit fees, audit-related fees and tax fees.

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

Pre-Approval Policies and Procedures

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

REPORT OF THE AUDIT COMMITTEE OF THE BOARD OF DIRECTORS

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

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

In the performance of its oversight function, the audit committee has considered and discussed the audited financial statements with management and our independent auditors. The committee has also discussed with our independent auditors the matters required to be discussed by Statement on Auditing Standards No. 61, Communication with Audit Committees, as currently in effect. Finally, the committee has received the written disclosures and the letter from the independent auditors required by Independence Standards Board Standard No. 1, Independence Discussions with Audit Committees, as currently in effect, and has discussed with the independent auditors their independence.

Based upon the reports and discussions described in this report, and subject to the limitations on the role and responsibilities of the audit committee referred to in the audit committee charter, the committee recommended to the board of directors that the audited financial statements be included in our annual report on Form 10-K for the year ended December 31, 2005.

AUDIT COMMITTEE

Clayton S. Rose (Chairman)
Samuel L. Barker, Ph.D.
Patricia M. Cloherty

The foregoing report of the audit committee shall not be deemed incorporated by reference by any general statement incorporating by reference this proxy statement into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate this information by reference, and shall not otherwise be deemed filed under such acts.

EXECUTIVE COMPENSATION

EXECUTIVE OFFICERS

The executive officers of the Company and their ages and positions are listed below.

| NAME | AGE | POSITION WITH THE COMPANY |
|------------------------------------|-----|---|
| Arthur T. Sands, M.D., Ph.D..... | 44 | President and Chief Executive Officer and Director |
| Julia P. Gregory..... | 53 | Executive Vice President, Corporate Development and Chief Financial Officer |
| Jeffrey L. Wade, J.D..... | 41 | Executive Vice President and General Counsel |
| Brian P. Zambrowicz, Ph.D..... | 43 | Executive Vice President of Research |
| Walter F. Colbert..... | 56 | Senior Vice President of Human Resources and Corporate Services |
| Lance K. Ishimoto, Ph.D., J.D..... | 46 | Senior Vice President of Intellectual Property |
| Alan J. Main, Ph.D..... | 52 | Senior Vice President, Lexicon Pharmaceuticals |
| James R. Piggott, Ph.D..... | 51 | Senior Vice President of Pharmaceutical Biology |

Information regarding the business experience of Dr. Sands is set forth above under the heading "Election of Directors-- Nominees for Class III Directors."

Julia P. Gregory has been our executive vice president, corporate development and chief financial officer since August 2003 and served as our executive vice president and chief financial officer from February 2000 until August 2003. From 1998 to February 2000, Ms. Gregory served as the head of investment banking for Punk, Ziegel & Company, a specialty investment banking firm focusing on technology and healthcare and, from 1996 to February 2000, as the head of the firm's life sciences practice. From 1980 to 1996, Ms. Gregory was an investment banker, primarily with Dillon, Read & Co., Inc., where she represented life sciences companies beginning in 1986. Ms. Gregory is a member of the board of directors and the scientific advisory board of the Estee Lauder Foundation's Institute for the Study of Aging, Inc. and a member of the International Council for George Washington University's Elliott School of International Affairs. She received her B.A. in international affairs from George Washington University and her M.B.A. from the Wharton School of the University of Pennsylvania.

Jeffrey L. Wade, J.D. has been our executive vice president and general counsel since February 2000 and was our senior vice president and chief financial officer from January 1999 to February 2000. From 1988 through December 1998, Mr. Wade was a corporate securities and finance attorney with the law firm of Andrews & Kurth L.L.P., for the last two years as a partner, where he represented companies in the biotechnology, information technology and energy industries. Mr. Wade is a member of the boards of directors of the Texas Healthcare and Bioscience Institute, the Texas Institute for Genomic Medicine and the Texas Life Science Center for Innovation and Commercialization. He received his B.A. and J.D. from the University of Texas.

Brian P. Zambrowicz, Ph.D. co-founded our company and has been our executive vice president of research since August 2002. Dr. Zambrowicz served as our senior vice president of genomics from February 2000 to August 2002, vice president of research from January 1998 to February 2000 and senior scientist from April 1996 to January 1998. From 1993 to April 1996, Dr. Zambrowicz served as a National Institutes of Health postdoctoral fellow at the Fred Hutchinson Cancer Center in Seattle, Washington, where he studied gene trapping and gene targeting technology. Dr. Zambrowicz is a member of the board of directors of the Texas Institute for Genomic Medicine. He received his B.S. in biochemistry from the University of Wisconsin. He received his Ph.D. from the University of Washington, where he studied tissue-specific gene regulation using transgenic mice.

Walter F. Colbert has been our senior vice president of human resources and corporate services since May 2002. Mr. Colbert served as our vice president of human resources from December 2000 to May 2002. From September 1997 to December 2000, Mr. Colbert was vice president, human resources and public affairs at the Sony Technology Center--San Diego of Sony Electronics Inc. From September 1995 to September 1997, Mr. Colbert served as vice president, human resources for The NutraSweet Kelco Company, Monsanto Company's food ingredients business unit. From 1976 through September 1995, Mr. Colbert served in a variety of human resources positions in the United States and Europe

with Ford Motor Company and Monsanto Company. He received his B.A. in political science from Stanford University and his M.A. in international affairs from the Fletcher School of Law and Diplomacy at Tufts University.

Lance K. Ishimoto, J.D., Ph.D. has been our senior vice president of intellectual property since February 2004. Dr. Ishimoto served as our vice president of intellectual property from July 1998 to February 2004. From 1994 to July 1998, Dr. Ishimoto was a biotechnology patent attorney at the Palo Alto, California office of the law firm of Pennie & Edmonds LLP. Dr. Ishimoto received his B.A. and Ph.D. from the University of California at Los Angeles, where he studied molecular mechanisms of virus assembly and the regulation of virus ultrastructure. After receiving his Ph.D., Dr. Ishimoto served as a National Institutes of Health postdoctoral fellow at the University of Washington School of Medicine. He received his J.D. from Stanford University.

Alan J. Main, Ph.D. has been our senior vice president, Lexicon Pharmaceuticals since July 2001. Dr. Main was president and chief executive officer of Coelacanth Corporation, a leader in using proprietary chemistry technologies to rapidly discover new chemical entities for drug development, from January 2000 until our acquisition of Coelacanth in July 2001. Dr. Main was formerly senior vice president, United States Research at Novartis Pharmaceuticals Corporation, where he worked for 20 years before joining Coelacanth. Dr. Main holds a B.S. from the University of Aberdeen, Scotland and a Ph.D. in organic chemistry from the University of Liverpool, England and completed postdoctoral studies at the Woodward Research Institute.

James R. Piggott, Ph.D. has been our senior vice president of pharmaceutical biology since January 2000. From 1990 through October 1999, Dr. Piggott worked for ZymoGenetics, Inc., a subsidiary of Novo Nordisk, a company focused on the discovery, development and commercialization of therapeutic proteins for the treatment of human disease, most recently as senior vice president-research biology from 1997 to October 1999. Dr. Piggott's pharmaceutical research experience also includes service at the Smith Kline & French Laboratories Ltd. unit of SmithKline Beecham plc and the G.D. Searle & Co. unit of Monsanto Company. Dr. Piggott received his B.A. and Ph.D. from Trinity College, Dublin.

SUMMARY COMPENSATION TABLE

The following table presents summary information for the years ended December 31, 2005, 2004 and 2003 regarding the compensation of each of our five most highly compensated executive officers.

| NAME AND POSITION | YEAR | ANNUAL COMPENSATION | | LONG-TERM | ALL OTHER |
|---|------|---------------------|-----------|---|-----------|
| | | SALARY | BONUS | COMPENSATION AWARDS SECURITIES UNDERLYING OPTIONS | |
| Arthur T. Sands, M.D., Ph.D. (2) President, Chief Executive Officer and Director | 2005 | \$473,000 | \$165,000 | 150,000 | \$6,045 |
| | 2004 | \$469,583 | \$205,244 | 150,000 | \$5,914 |
| | 2003 | \$432,000 | \$309,536 | 135,000 | \$6,022 |
| Julia P. Gregory Executive Vice President Corporate Development and Chief Financial Officer | 2005 | \$329,000 | \$ 80,000 | 75,000 | \$5,803 |
| | 2004 | \$327,417 | \$ 98,891 | 75,000 | \$5,675 |
| | 2003 | \$286,000 | \$126,215 | 72,000 | \$5,711 |
| Jeffrey L. Wade, J.D. Executive Vice President and General Counsel | 2005 | \$292,000 | \$ 80,000 | 60,000 | \$5,741 |
| | 2004 | \$289,854 | \$ 79,190 | 60,000 | \$5,612 |
| | 2003 | \$266,250 | \$100,630 | 54,000 | \$5,631 |
| Brian P. Zambrowicz, Ph.D. Executive Vice President of Research | 2005 | \$312,000 | \$ 90,000 | 70,000 | \$5,774 |
| | 2004 | \$309,750 | \$102,665 | 70,000 | \$5,645 |
| | 2003 | \$285,000 | \$109,140 | 63,000 | \$5,674 |
| Alan J. Main, Ph.D. Senior Vice President, Lexicon Pharmaceuticals | 2005 | \$312,000 | \$ 60,000 | 50,000 | \$5,774 |
| | 2004 | \$310,754 | \$ 80,384 | 50,000 | \$5,647 |
| | 2003 | \$297,045 | \$ 83,780 | 54,000 | \$5,674 |

(1) Other compensation during 2005, 2004 and 2003 includes the following amounts in respect of company matching contributions under our 401(k) plan and company-paid premiums for group term life insurance. The company-paid life insurance premiums reflect payments for group term life policies maintained for the benefit of all employees.

| | YEAR | COMPANY 401(K) MATCHING CONTRIBUTION | COMPANY-PAID GROUP TERM LIFE INSURANCE PREMIUMS |
|----------------------------------|------|--|---|
| Arthur T. Sands, M.D., Ph.D..... | 2005 | \$5,250 | \$ 795 |
| | 2004 | \$5,125 | \$ 789 |
| | 2003 | \$5,000 | \$1,022 |
| Julia P. Gregory..... | 2005 | \$5,250 | \$ 553 |
| | 2004 | \$5,125 | \$ 550 |
| | 2003 | \$5,000 | \$ 711 |
| Jeffrey L. Wade, J.D..... | 2005 | \$5,250 | \$ 491 |
| | 2004 | \$5,125 | \$ 487 |
| | 2003 | \$5,000 | \$ 631 |
| Brian P. Zambrowicz, Ph.D..... | 2005 | \$5,250 | \$ 524 |
| | 2004 | \$5,125 | \$ 520 |
| | 2003 | \$5,000 | \$ 674 |
| Alan J. Main, Ph.D..... | 2005 | \$5,250 | \$ 524 |
| | 2004 | \$5,125 | \$ 522 |
| | 2003 | \$5,000 | \$ 674 |

(2) The amount reflected as bonus compensation for Dr. Sands in 2003 includes a bonus payment to Dr. Sands of \$59,706 to enable him to make, for his own account, the minimum premium payments required for him to maintain the split-dollar life insurance arrangement previously required under his employment agreement with us. We will not receive any cash under the policy upon Dr. Sands' death in respect of such bonus amount or the premiums paid by Dr. Sands, for his own account, under such policy.

OPTION GRANTS IN 2005

The following table presents each grant of stock options in 2005 to the individuals named in the summary compensation table.

| NAME | NUMBER OF SECURITIES UNDERLYING OPTIONS GRANTED | PERCENTAGE OF TOTAL OPTIONS GRANTED TO EMPLOYEES IN 2005 | EXERCISE PRICE PER SHARE | EXPIRATION DATE | POTENTIAL REALIZABLE VALUE AT ASSUMED ANNUAL RATES OF STOCK PRICE APPRECIATION FOR OPTION TERM | |
|----------------------------------|---|--|-----------------------------------|--------------------|---|-------------|
| | | | | | 5% | 10% |
| Arthur T. Sands, M.D., Ph.D..... | 150,000 | 7.3% | \$5.76 | 2/18/2015 | \$543,365 | \$1,376,993 |
| Julia P. Gregory..... | 75,000 | 3.7% | \$5.76 | 2/18/2015 | \$271,682 | \$ 688,497 |
| Jeffrey L. Wade, J.D..... | 60,000 | 2.9% | \$5.76 | 2/18/2015 | \$217,346 | \$ 550,797 |
| Brian P. Zambrowicz, Ph.D..... | 70,000 | 3.4% | \$5.76 | 2/18/2015 | \$253,570 | \$ 642,597 |
| Alan J. Main, Ph.D..... | 50,000 | 2.4% | \$5.76 | 2/18/2015 | \$181,122 | \$ 458,998 |

The exercise price of each of the options in the foregoing table was equal to the fair market value of our common stock as determined by our board of directors on the date of grant. The exercise price for each option may be paid in cash or in shares of our common stock valued at fair market value on the exercise date or through a cashless exercise procedure involving a same-day sale of the purchased shares.

The potential realizable value of these options is calculated based on the ten-year term of the option at the time of grant. Stock price appreciation of 5% and 10% is assumed pursuant to rules promulgated by the Securities and Exchange Commission and does not represent our prediction of our stock price performance.

Percentages shown under "Percentage of Total Options Granted to Employees in 2005" are based on an aggregate of 2,044,100 options granted to our employees under our 2000 Equity Incentive Plan during 2005.

AGGREGATED OPTION EXERCISES IN 2005 AND OPTION VALUES AT DECEMBER 31, 2005

The following table presents information about:

- option exercises in 2005 by each of the individuals listed in the summary compensation table; and
- the number and value of the shares of common stock underlying unexercised options that are held by each of the individuals listed in the summary compensation table as of December 31, 2005.

Amounts shown under the column "Value Realized" are based on the market price of our common stock on the date of exercise, without taking into account any taxes that may be payable in connection with the transaction, less the exercise price paid for the purchased shares.

Amounts shown under the column "Value of Unexercised In-the-Money Options at December 31, 2005" are based on the closing price of our common stock on The Nasdaq National Market on December 30, 2005 of \$3.65 per share, without taking into account any taxes that may be payable in connection with the transaction, less the exercise price payable for these shares.

| NAME | SHARES ACQUIRED ON EXERCISE | VALUE REALIZED | NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS AT DECEMBER 31, 2005 | | VALUE OF UNEXERCISED IN-THE-MONEY OPTIONS AT DECEMBER 31, 2005 | |
|----------------------------------|--------------------------------------|-------------------|---|---------------|--|---------------|
| | | | EXERCISABLE | UNEXERCISABLE | EXERCISABLE | UNEXERCISABLE |
| Arthur T. Sands, M.D., Ph.D..... | 682,500 | \$3,221,175 | 2,182,359 | 277,641 | \$2,268,240 | -- |
| Julia P. Gregory..... | -- | -- | 664,660 | 140,340 | \$ 497,950 | -- |
| Jeffrey L. Wade, J.D..... | -- | -- | 685,567 | 110,933 | \$ 583,625 | -- |
| Brian P. Zambrowicz, Ph.D..... | 95,000 | \$ 427,184 | 978,614 | 129,386 | \$ 971,997 | -- |
| Alan J. Main, Ph.D..... | -- | -- | 424,556 | 93,445 | \$ 82,322 | -- |

EMPLOYMENT AGREEMENTS

In October 1999, we entered into an employment agreement with Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, which was subsequently restated in February 2006. Under the agreement, Dr. Sands receives a base salary, currently \$473,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides that if we terminate Dr. Sands' employment without cause or Dr. Sands voluntarily terminates his employment for good reason, we will pay him his then-current salary for 12 months.

In February 2000, we entered into an employment agreement with Julia P. Gregory to serve as our executive vice president and chief financial officer starting in February 2000. In August 2003, Ms. Gregory was named executive vice president, corporate development and chief financial officer. Under the agreement, Ms. Gregory receives a base salary, currently \$329,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides that if we terminate Ms. Gregory's employment without cause or Ms. Gregory voluntarily terminates her employment for good reason, we will pay her then-current salary for six months. If any such termination follows a change in control of our company, we will pay Ms. Gregory her then-current salary for 12 months.

In December 1998, we entered into an employment agreement with Jeffrey L. Wade, J.D. to serve as our senior vice president and chief financial officer starting in January 1999. In February 2000, Mr. Wade was named executive vice president and general counsel. Under the agreement, Mr. Wade receives a base salary, currently \$292,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides that if we terminate Mr. Wade's employment without cause or Mr. Wade voluntarily terminates his employment for good reason, we will pay him his then-current salary for six months. If any such termination follows a change in control of our company, we will pay Mr. Wade his then-current salary for 12 months.

In February 2000, we entered into an employment agreement with Brian P. Zambrowicz, Ph.D., then our senior vice president of genomics. In August 2002, Dr. Zambrowicz was named executive vice president of research. Under the agreement, Dr. Zambrowicz receives a base salary, currently \$312,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides that if we terminate Dr. Zambrowicz's employment without cause or Dr. Zambrowicz voluntarily terminates his employment for good reason, we will pay him his then-current salary for six months. If any such termination follows a change in control of our company, we will pay Dr. Zambrowicz his then-current salary for 12 months.

In July 2001, we entered into an employment agreement with Alan J. Main, Ph.D., our senior vice president, Lexicon Pharmaceuticals. Under the agreement, Dr. Main receives a base salary, currently \$312,000 a year, subject to adjustment, with an annual discretionary bonus based upon specific objectives to be determined by the compensation committee. The employment agreement is at-will and contains a non-competition agreement. The agreement also provides that if we terminate Dr. Main's employment without cause or Dr. Main voluntarily terminates his employment for good reason, we will pay him his then-current salary for six months. If any such termination follows a change in control of our company, we will pay Dr. Main his then-current salary for 12 months.

REPORT OF THE COMPENSATION COMMITTEE OF THE BOARD OF DIRECTORS

The compensation committee of our board of directors is responsible for evaluating the performance of management, determining the compensation of our executive and other officers and administering our 2000 Equity Incentive Plan, under which stock option grants and other stock awards may be made to our employees. The committee has furnished the following report on executive compensation for 2005:

Executive Compensation Policies and Practices

Under the supervision of the compensation committee, our company has developed a compensation policy that is designed to attract and retain key executives responsible for our success and motivate management to enhance long-term stockholder value. The annual compensation package for executive and other officers primarily consists of:

- a base salary, which reflects the responsibilities relating to the position and individual performance;
- variable annual cash bonus awards tied to the achievement of specified individual and corporate goals and milestones; and
- long-term stock-based incentive awards which strengthen the mutuality of interests between our executive and other officers and our stockholders.

The committee generally seeks to set targeted total cash compensation, consisting of base salaries and annual cash bonus award targets, at or slightly above the median of a peer group of biopharmaceutical companies if such compensation level is justified by company performance, individual performance and prevailing financial conditions. Historically, the committee did not establish specific targets for total direct compensation, consisting of targeted total cash compensation and long-term stock-based incentive awards, but generally sought to set such total direct compensation at or above the median of our peer group companies. After a review of our compensation policies and practices conducted in 2005, the committee revised our compensation policy to reflect that, prospectively, it is the committee's intention to set total direct compensation at or near the 75th percentile of our peer group companies if such compensation level is justified by company performance, individual performance and prevailing financial conditions. Taking these factors into account with respect to 2005, the committee sought, in making compensation decisions in February 2006, to set total direct compensation for the officer group as a whole at or near the 60th percentile of our peer group companies. In reviewing comparative data and making compensation determinations, the committee reviews total direct compensation in its totality, assigning dollar values to each of the elements of such compensation, including base salary, annual cash bonus award targets and long-term stock-based incentive awards.

In determining peer group compensation, the committee uses available survey data from several sources, relying principally on data from a comprehensive survey of the compensation practices of several hundred companies in the biopharmaceutical industry. The committee supplements this survey data with reviews of the publicly-disclosed compensation practices of a group of biopharmaceutical companies selected for comparison purposes based on one or more factors, including number of employees, revenues, stage of development, and location of principal operations. In 2005, this group of companies consisted of Abgenix, Inc., Arqule, Inc., Curagen Corporation, Exelixis, Inc., Gene Logic Inc., Human Genome Sciences, Inc., Incyte Corporation, Medarex, Inc., Millennium Pharmaceuticals, Inc., Myriad Genetics, Inc., PDL Biopharma, Inc., Tanox, Inc., Transkaryotic Therapies, Inc., Vertex Pharmaceuticals Incorporated and ZymoGenetics, Inc. The peer group of biopharmaceutical companies for which we obtained survey data and the additional group of companies listed above do not necessarily coincide with the companies comprising the Nasdaq Biotechnology Index reflected in the performance graph in this proxy statement.

In determining the level and composition of compensation of each of our executive and other officers, the committee takes into account various qualitative and quantitative indicators of corporate and individual performance. Because our business and technology are continuing to develop, the use of certain traditional performance standards, such as profitability and return on equity, are not currently appropriate in evaluating the performance of our executive and other officers. Consequently, in evaluating the performance of management, the committee takes into consideration such factors as the development of drug candidates, the identification of novel drug targets and other goals related to our research and development programs, and our achievement of specified milestones and goals with respect to cash, revenues and new business development. In addition, the committee recognizes performance and achievements that are more difficult to quantify, such as the successful supervision of major corporate projects and demonstrated leadership ability.

Company Performance Criteria

The committee generally makes executive compensation determinations in February of each year, taking into account company and individual performance over the preceding year, as well as prevailing financial conditions. In February 2005, the committee made determinations regarding 2004 bonus awards and 2005 base salaries and annual stock option grants, taking into account the following factors in its evaluation of corporate performance in 2004: our progress relative to our objectives in advancing our drug research and development programs; the increase in our revenues for 2004 as compared to 2003; our establishment of a new drug discovery alliance with Takeda Pharmaceutical Company Limited and our performance under existing drug discovery alliances with Bristol-Myers Squibb Company and Genentech, Inc.; our performance relative to our objectives for cash; and the performance of our stock price over the course of the year. In February 2006, the committee made determinations regarding 2005 bonus awards and 2006 base salaries and annual stock option grants, taking into account the following factors in its evaluation of corporate performance in 2005: our progress relative to our objectives in advancing our drug research and development programs; the increase in our revenues for 2005 as compared to 2004; our establishment of a number of substantial new or expanded alliances and collaborations, including a drug discovery alliance with N.V. Organon, an expanded drug discovery alliance with Genentech, Inc., and an award from the Texas Enterprise Fund for the creation of a knockout mouse embryonic stem cell library for the Texas Institute for Genomic Medicine; our receipt of sufficient cash in connection with such alliances and collaborations, as well as from other contracts and licenses, to result in an increase in cash at year-end over the prior year; and the performance of our stock price over the course of the year.

Compensation Consultant

The committee is granted the authority under its charter to retain compensation consultants or other advisors to assist in its evaluation of executive compensation. Consistent with such authority, the committee retained Aon Consulting, Inc. in 2005 as an independent compensation consultant to advise the committee on matters relating to executive compensation. At the committee's request, Aon participated in meetings with the committee and its members, conducted interviews of executive and other officers, and prepared a competitive assessment and market analysis of our executive compensation for the committee's benefit. The consultant was engaged by and responsible to the committee and, except for fees of less than \$7,500 paid to an affiliated entity for two annual compensation surveys and a benefits survey, has not received any compensation from us for services other than those performed for the committee under such engagement. The committee used the results of the consultant's market analysis in making compensation decisions for 2006.

Base Compensation

Base compensation of executive and other officers is established through negotiation between the company and the officer at the time he or she is hired, and then subsequently adjusted when the officer's base compensation is subject to review or reconsideration. While we have entered into employment agreements with certain of our executive officers, these agreements provide that base salaries after the initial year will be reviewed and determined by the committee. When establishing base salary levels for executive and other officers, the committee, in accordance with its general compensation policy, considers numerous factors, including the responsibilities relating to the position, the qualifications of the executive and the relevant experience the individual brings to the company, strategic goals for which the executive has responsibility, and compensation levels of companies at a comparable stage of development who compete with us for business, scientific and executive talents. When considering increases to base salary levels for officers, which typically

occurs each February, the committee considers individual and company performance in addition to the foregoing factors. No pre-determined weights are given to any one of these factors.

The base salaries of each of our executive officers remained unchanged in 2005 from the rate established in February 2004 and were competitive with those paid by our peer group companies, with most falling near the median for such peer group companies. In establishing base salaries for 2005, the committee considered the competitiveness of our cash compensation arrangements for executive officers and our cash position and needs for the year.

Incentive Compensation

Cash Bonus Awards

In addition to base salary, the committee may award variable annual cash bonus awards to chosen executive and other officers depending on the extent to which certain predefined corporate and personal performance goals are achieved. These performance goals include those discussed generally above, as well as strategic and operational goals for the company as a whole. The committee typically considers the award of cash bonuses each February relating to performance for the preceding year. For each of our officers, the committee establishes a bonus target, expressed as a percentage of base salary, which is used to determine the cash bonus amount, assuming that corporate and individual goals are fully achieved.

In determining the cash bonus awards paid in February 2006 with respect to 2005 performance, the committee included the relevant factors described above under "-- Company Performance Criteria" in its evaluation of corporate performance. After taking into account these factors, the committee determined that our objectives for the year had been partially but not fully achieved, and awarded bonuses for 2005 in amounts reflecting such partial achievement.

Stock-Based Awards

All of our employees, including our executive and other officers, are eligible to receive long-term stock-based incentive awards under our 2000 Equity Incentive Plan as a means of providing such individuals with a continuing proprietary interest in our success. These grants are typically awarded each February and align the interests of our employees and our stockholders by providing significant incentives for our employees to achieve and maintain high levels of performance. Our 2000 Equity Incentive Plan enhances our ability to attract and retain the services of qualified individuals. Factors considered in determining whether and in what amounts such awards are granted to an officer include the executive's position, his or her performance and responsibilities, the amount of stock options currently held by the officer, the vesting schedules of any such options and the officer's other compensation. While the committee does not adhere to any firmly established formulas or schedules for the issuance of awards such as options or restricted stock, the committee takes into account, in making award decisions, the total direct compensation objectives described above. In addition, the committee will generally tailor the terms of any such grant to achieve its goal as a long-term incentive award by providing for a vesting schedule encompassing several years.

In February 2005, the committee approved annual stock option grants to executive officers and other employees who satisfied eligibility requirements, including time of service. In making such grants, the committee considered corporate and individual performance in 2004, total direct compensation objectives for individual officers, and information regarding stock option grants made by other companies in the biotechnology industry.

Compensation of the Chief Executive Officer

The annual base salary of Arthur T. Sands, M.D., Ph.D., our president and chief executive officer, was \$473,000 for 2005, unchanged from the rate established in February 2004. In electing to leave Dr. Sands' base salary unchanged from the preceding year, the committee considered the competitiveness of his base salary and our cash position and needs for 2005.

In February 2006, the committee awarded a bonus to Dr. Sands for 2005 in the amount of \$165,000 on the basis of his and the company's achievements in 2005 relative to performance goals established at the outset of the year. These performance goals included objectives regarding the development of drug candidates, the identification of novel drug targets and other goals related to our research and development programs, and the achievement of specified milestones and goals with respect to cash, revenue, new business development and stock price performance. The committee

determined that our corporate objectives for the year had been partially but not fully achieved, as described in more detail above, and awarded Dr. Sands a bonus for 2005 in an amount reflecting such partial achievement. At the same time, the committee elected to leave Dr. Sands' annual base salary for 2006 unchanged from 2005.

The committee granted a stock option to Dr. Sands in February 2005, at the same time annual grants were made to other employees. The stock option entitles Dr. Sands to purchase an aggregate of 150,000 shares of common stock at an exercise price of \$5.76 per share. In making the option grant to Dr. Sands, the committee considered corporate and individual performance in 2004, total direct compensation objectives for Dr. Sands, and information regarding stock option grants made by other companies in the biotechnology industry.

Section 162(m)

Section 162(m) of the Internal Revenue Code places a \$1 million cap per executive on the deductible compensation that can be paid to certain executives of publicly-traded corporations. Amounts that qualify as "performance based" compensation under Section 162(m)(4)(c) of the Code are exempt from the cap and do not count toward the \$1 million limit. Generally, stock options will qualify as performance based compensation. The committee has discussed and considered and will continue to evaluate the potential impact of Section 162(m) on the company in making compensation determinations, but has not established a set policy with respect to future compensation determinations.

COMPENSATION COMMITTEE

Clayton S. Rose (Chairman)
 Samuel L. Barker, Ph.D.
 Frank P. Palantoni

The foregoing report of the compensation committee shall not be deemed incorporated by reference by any general statement incorporating by reference this proxy statement into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate this information by reference, and shall not otherwise be deemed filed under such acts.

PERFORMANCE GRAPH

The following performance graph compares the performance of our common stock to the Nasdaq Composite Index and the Nasdaq Biotechnology Index for the period beginning December 31, 2000 and ending December 31, 2005. The graph assumes that the value of the investment in our common stock and each index was \$100 at December 31, 2000, and that all dividends were reinvested.

(PERFORMANCE GRAPH)

| | DECEMBER 31, | | | | | |
|-------------------------------|--------------|------|------|------|------|------|
| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 |
| Lexicon Genetics Incorporated | 100 | 69 | 28 | 35 | 47 | 22 |
| Nasdaq Composite Index | 100 | 79 | 54 | 81 | 88 | 89 |
| Nasdaq Biotechnology Index | 100 | 84 | 46 | 67 | 71 | 73 |

The foregoing stock price performance comparisons shall not be deemed incorporated by reference by any general statement incorporating by reference this proxy statement into any filing under the Securities Act of 1933 or under the Securities Exchange Act of 1934, except to the extent that we specifically incorporate such comparisons by reference, and shall not otherwise be deemed filed under such acts.

PROPOSALS OF STOCKHOLDERS

In order for a stockholder proposal to be considered for inclusion in our proxy statement for next year's annual meeting, we must receive the written proposal at our principal executive offices no later than November 24, 2006. Any such proposal must also comply with Securities and Exchange Commission regulations regarding the inclusion of stockholder proposals in company-sponsored proxy materials. Similarly, in order for any stockholder proposal to be otherwise raised during next year's annual meeting, we must receive written notice of the proposal, containing the information required by our bylaws, at our principal executive offices no later than November 24, 2006. You may contact the corporate secretary at our principal executive offices for a copy of the relevant bylaw provisions for making stockholder proposals.

FINANCIAL INFORMATION

Our annual report to stockholders, including financial statements, accompanies this proxy statement but does not constitute a part of the proxy solicitation materials. YOU MAY OBTAIN, WITHOUT CHARGE, A COPY OF OUR ANNUAL REPORT ON FORM 10-K, INCLUDING THE FINANCIAL STATEMENTS AND EXHIBITS THERETO, BY WRITTEN REQUEST TO CORPORATE COMMUNICATIONS, LEXICON GENETICS INCORPORATED, 8800 TECHNOLOGY FOREST PLACE, THE WOODLANDS, TEXAS 77381.

By order of the board of directors,

/s/ Jeffrey L. Wade

Jeffrey L. Wade
Secretary

March 24, 2006
The Woodlands, Texas

LEXICON GENETICS INCORPORATED
AUDIT COMMITTEE CHARTER

GENERAL PURPOSE

The Audit Committee of Lexicon Genetics Incorporated (the "Company") is appointed by the board of directors of the Company (the "Board") to assist the Board in monitoring (1) the integrity of the financial statements of the Company, (2) the independent auditor's qualifications and independence, (3) the performance of the Company's independent auditors and (4) the compliance by the Company with legal and regulatory requirements.

COMMITTEE MEMBERSHIP

The Audit Committee shall consist of no fewer than three members. The members of the Audit Committee shall meet the independence and experience requirements of The Nasdaq Stock Market, Inc. (or any other exchange on which the Company's securities are listed) and the Securities Exchange Act of 1934, including all rules and regulations promulgated thereunder (the "Exchange Act"). At least one member of the Audit Committee shall be an "audit committee financial expert" as defined by the rules of the Securities and Exchange Commission (the "Commission"). The members of the Audit Committee shall be appointed or replaced by the Board on the recommendation of the Chairman of the Board.

MEETINGS

The Audit Committee shall meet as often as it determines, but not less frequently than quarterly. The Audit Committee shall meet periodically with management and the independent auditor in separate executive sessions. The Audit Committee may request any officer or employee of the Company or the Company's outside counsel or independent auditor to attend a meeting of the Committee or to meet with any members of, or advisors to, the Committee.

COMMITTEE AUTHORITY AND RESPONSIBILITIES

The Audit Committee shall have the sole authority to appoint or replace the independent auditor (subject, if applicable, to shareholder ratification). The Audit Committee shall be directly responsible for the determination of appropriate compensation and oversight of the work of the independent auditor (including resolution of disagreements between management and the independent auditor regarding financial reporting) for the purpose of preparing or issuing an audit report or related work. The independent auditor shall report directly to the Audit Committee.

The Audit Committee shall preapprove all auditing services and permitted non-audit services (including the fees and terms thereof) to be performed for the Company by its independent auditor, subject to the de minimis exceptions for non-audit services described in Section 10A(i)(1)(B) of the Exchange Act which are approved by the Audit Committee prior to the completion of the audit. The Audit Committee may form and delegate authority to subcommittees consisting of one or more members when appropriate, including the authority to grant preapprovals of audit and permitted non-audit services, provided that decisions of such subcommittee to grant preapprovals shall be presented to the full Audit Committee at its next scheduled meeting.

The Audit Committee shall have the authority, to the extent it deems necessary or appropriate, to retain independent legal, accounting or other advisors.

The Company shall provide for appropriate funding, as determined by the Audit Committee, for payment of compensation to the independent auditor for the purpose of rendering or issuing an audit report or related work and to any advisors retained by the Audit Committee.

The Audit Committee shall make regular reports to the Board and shall prepare the report required by the Exchange Act to be included in the Company's annual proxy statement. The Audit Committee shall review and reassess

the adequacy of this Charter annually and recommend any proposed changes to the Board for its approval. The Audit Committee shall annually review the Audit Committee's own performance.

In carrying out its duties, the Audit Committee relies upon management and the independent auditor to provide relevant information and raise appropriate issues and concerns on a timely basis.

The Audit Committee, to the extent it deems necessary or appropriate, shall:

Financial Statement and Disclosure Matters

1. Review and discuss with management and the independent auditor the annual audited financial statements, including disclosures made in management's discussion and analysis, and recommend to the Board whether the audited financial statements should be included in the Company's Form 10-K.

2. Review and discuss with management and the independent auditor the Company's quarterly financial statements prior to the filing of its Form 10-Q, including the results of the independent auditor's review of the quarterly financial statements.

3. Discuss with management and the independent auditor significant financial reporting issues and judgments made in connection with the preparation of the Company's financial statements, including any significant changes in the Company's selection or application of accounting principles, any major issues as to the adequacy of the Company's internal controls and any special steps adopted in light of material control deficiencies.

4. Review and discuss quarterly reports from the independent auditors on:

(a) All critical accounting policies and practices to be used.

(b) All alternative treatments of financial information within generally accepted accounting principles that have been discussed with management, ramifications of the use of such alternative disclosures and treatments, and the treatment preferred by the independent auditor.

(c) Other material written communications between the independent auditor and management, such as any management letter or schedule of unadjusted differences.

5. Discuss with management the Company's earnings press releases, including the use of "pro forma" or "adjusted" non-GAAP information.

6. Discuss with management and the independent auditor the selection and application of accounting principles for the Company's significant transactions.

7. Discuss with management and the independent auditor the effect of financial, regulatory and accounting initiatives as well as off-balance sheet structures on the Company's financial statements.

8. Discuss with management the Company's major financial risk exposures and the steps management has taken to monitor and control such exposures, including the Company's risk assessment and risk management policies.

9. Discuss with the independent auditor the matters required to be discussed by Statement on Auditing Standards No. 61 relating to the conduct of the audit, including any difficulties encountered in the course of the audit work, any restrictions on the scope of activities or access to requested information, and any significant disagreements with management.

10. Review disclosures made to the Audit Committee by the Company's CEO and CFO during their certification process for the Form 10-K and Form 10-Q about any significant deficiencies in the design or operation of internal controls or material weaknesses therein and any fraud involving management or other employees who have a significant role in the Company's internal controls.

Oversight of the Company's Relationship with the Independent Auditor

11. Review and evaluate the lead partner of the independent auditor team.

12. Obtain and review a report from the independent auditor at least annually regarding (a) the independent auditor's internal quality-control procedures, (b) any material issues raised by the most recent internal quality-control review, or peer review, of the firm, or by any inquiry or investigation by governmental or professional authorities within the preceding five years respecting one or more independent audits carried out by the firm, (c) any steps taken to deal with any such issues, and (d) all relationships between the independent auditor and the Company. Evaluate the qualifications, performance and independence of the independent auditor, including considering whether the auditor's quality controls are adequate and the provision of permitted non-audit services is compatible with maintaining the auditor's independence, taking into account the opinions of management. The Audit Committee shall present its conclusions with respect to the independent auditor to the Board.

13. Ensure the rotation of the audit partners as required by law. Consider whether, in order to assure continuing auditor independence, it is appropriate to adopt a policy of rotating the independent auditing firm on a regular basis.

14. Meet with the independent auditor prior to the audit to discuss the planning and staffing of the audit.

Compliance Oversight Responsibilities

15. Obtain from the independent auditor assurance that, in the course of conducting the audit, it has not detected or otherwise become aware of information indicating that any illegal act (whether or not having a material effect on the financial statements of the Company) has or may have occurred.

16. Obtain reports from management and the independent auditor that the Company and its subsidiary/foreign affiliated entities are in conformity with applicable legal requirements and the Company's internal policies. Review reports and disclosures of insider and affiliated party transactions. Advise the Board with respect to the Company's policies and procedures regarding compliance with applicable laws and regulations and with the Company's internal policies.

17. Establish procedures for the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting or auditing matters.

18. Discuss with management and the independent auditor any correspondence with regulators or governmental agencies and any published reports which raise material issues regarding the Company's financial statements or accounting policies.

19. Discuss with the Company's General Counsel legal matters that may have a material impact on the financial statements or the Company's compliance policies.

The Audit Committee shall also have such other authority and responsibilities as may be determined from time to time by the Board.

LIMITATION OF AUDIT COMMITTEE'S ROLE

While the Audit Committee has the authority and responsibilities set forth in this Charter, it is not the duty of the Audit Committee to (1) plan or conduct audits, (2) determine that the Company's financial statements and disclosures are complete, accurate and fairly presented and are in accordance with generally accepted accounting principles and applicable rules and regulations or (3) assure compliance with the Company's internal controls and policies. These are the responsibilities of management or the independent auditor.

PROXY

LEXICON GENETICS INCORPORATED

ANNUAL MEETING OF STOCKHOLDERS
APRIL 26, 2006

THIS PROXY IS SOLICITED ON BEHALF OF THE BOARD OF DIRECTORS OF
LEXICON GENETICS INCORPORATED

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 Annual Meeting of Stockholders of Lexicon Genetics Incorporated (the "Company") to be held at The Marriott Woodlands Waterway Hotel and Convention Center, 1601 Lake Robbins Drive, The Woodlands, Texas, on April 26, 2006, 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 GENETICS INCORPORATED ACCOUNT ONLINE.

Access your Lexicon Genetics Incorporated stockholder account online via Investor ServiceDirect(R) (ISD).

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

- - View account status
- - View certificate history
- - View book-entry information
- View payment history for dividends
- Make address changes
- Obtain a duplicate 1099 tax form
- Establish/change your PIN

VISIT US ON THE WEB AT [HTTP://WWW.MELLONINVESTOR.COM](http://www.melloninvestor.com)

FOR TECHNICAL ASSISTANCE CALL 1-877-978-7778 BETWEEN 9AM-7PM
MONDAY-FRIDAY EASTERN TIME

INVESTOR SERVICEDIRECT(R) IS A REGISTERED TRADEMARK OF MELLON
INVESTOR SERVICES LLC

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 election of the nominees for Class III Director; and
"FOR" the proposal to ratify and approve the appointment of Ernst & Young LLP as the Company's independent public accountants for the fiscal year ending December 31, 2006.

2. Ratification and approval of the appointment of Ernst & Young LLP as the Company's independent auditors for the fiscal year ending December 31, 2006. FOR [] AGAINST [] ABSTAIN []

1. Election of Class III Directors

Nominees:
01 Arthur T. Sands, M.D., Ph.D.
02 Frank Palantoni

FOR all nominees listed except as indicated []

WITHHOLD AUTHORITY to vote for all nominees []

If You plan to attend the meeting in person, please mark the following box. []

INSTRUCTION: To withhold authority to vote for any individual nominee, write that nominee's name on the following line.

Dated _____, 2006

(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